MEDICAL PROCEEDINGS

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EDITORIAL · REDAKSIONEEL

PLASMA VERSUS DEXTRAN

The need for a plasma substitute which could be produced in large quantities arose from the knowledge gained during World War I of the treatment of oligaemic shock by blood transfusion. At that time, the methods of preserving blood were still undeveloped and an attempt was made to supplement supplies of whole blood with fluids such as solutions of gum acacia and of gelatin. World War II gave further impetus to the search for an effective plasma substitute because of the fear that supplies of blood and plasma might prove to be insufficient for the treatment of the large numbers of casualties expected—a fear which proved to be largely unfounded thanks to the highly developed organization for obtaining blood and plasma. The phenomenal results achieved in the treatment of shock and haemorrhage by transfusion of blood and plasma stimulated interest further in the development of safe and effective transfusion fluids which for financial, climatic and other reasons could not be met by the provision of human blood. The ever-increasing destructive capacity of modern instruments of warfare has served to re-awaken the fear that, in any future conflict, the needs and the difficulties of organizing and maintaining adequate supplies of blood and plasma may be even greater than they were in World War II.

The development of macro-molecular solutions (e.g. polyvinylpyrrolidone and dextran) represents progress towards an effective substitute in those conditions for which blood and plasma would normally be used.

It is greatly to the credit of the manufacturers of these plasma substitutes that they have never claimed that their products are

PLASMA VERSUS DEKSTRAN

Die behoefte aan 'n plasma-plaasvervanger wat in groot hoeveelhede geproduseer kan word, het ontstaan uit die kennis in verband met die behandeling van oligemiese skok met behulp van bloedoortappings wat tydens Wêreldoorlog I opgedoen is. In daardie jare was bloedbewaringsmetodes nog onontwikkel, en 'n poging is aangewend om die voorraad heelbloed aan te vul met vloeistowwe soos oplossings van akasiagom en van gelatien. Wêreldoorlog II het verdere stukrag aan die soektog na 'n doeltreffende plasma-vervanger gegee, want daar het vrees bestaan dat die voorrade bloed en plasma miskien nie voldoende sou wees vir die behandeling van die groot aantal ongevalle wat verwag is nie. Hierdie vrees het geblyk in 'n groot mate ongegrond te wees, danksy die hoogs ontwikkelde organisasie vir die verkryging van bloed en plasma. Die fenomenale resultate wat behaal is by die behandeling van skok en bloeding met behulp van bloed- en plasma-oortappings het verdere belangstelling aangewakker in die ontwikkeling van veilige en doeltreffende oortappingsvloeistowwe vir daardie gevalle waar menslike bloed om finansiële, klimaats- en ander redes nie beskikbaar gestel kon word nie. Die steeds toenemende vernietigingsvermoë van moderne krygstuig het weer eens die vrees laat ontstaan dat, in enige toekomstige oorlog, die behoefte en die moeilikhede verbonde aan die organisasie en instandhouding van doeltreffende hoeveelhede bloed en plasma, miskien groter sal wees as wat hulle in Wêreldoorlog II was.

Die ontwikkeling van makromolekulêre oplossings (bv. polivinielpirrolidoon en dekstran) was vooruitgang in die rigting van 'n doelmatige plaasvervanger vir toestande waar bloed

equivalent to human plasma either chemically or physiologically.

In our Correspondence columns in this issue Dr. S. G. Rainsford criticizes our Editorial of 23 November 1957. He has clearly set out to prove that dextran is not only equivalent to plasma but, in some respects, even superior to it. In doing this he has gone very much further than any living authority on the subject and it therefore becomes necessary to evaluate his claims and his criticisms.

In the first place, it must be emphasized that our Editorial was intended to underline the important announcement that blood plasma is now being made freely available to practitioners throughout the Union by the South African Blood Transfusion Service. Nothing was contained in that Editorial which decried the use of plasma substitutes in emergency situations such as war or even in civilian practice when human blood and plasma might be unavailable or available in insufficient supply. The point was however made that not one of the so-called plasma substitutes so far offered could be regarded as adequate and in support of our contention the eminent authority of the authors of *Dextran, Its Properties and Use in Medicine* was quoted. A further quotation from the same work (at p. 7) should serve to clarify the legitimate role of 'plasma savers' in practice.

'Dextran solutions and other plasma substitutes probably have their greatest part to play (1) in normal transfusion practice while waiting for compatibility tests, and *when plasma is not available* (italics inserted), (2) in places where adequate transfusion services do not exist for climatic, geographical or financial reasons and (3) in national emergencies.'

We also stated that the plasma now made available in South Africa is prepared on a unit-for-unit basis from the 'surplus of unused blood', i.e. from blood in excess of immediate requirements, not from 'time-expired blood'. The dating period for whole blood in acid-citrate-dextrose solution is generally regarded as 3 weeks; in many places this is even extended to 4 weeks. To ensure that blood is used as freshly as possible, the dating period in the South African Blood Transfusion Service has been reduced to 2 weeks. The plasma which the Service prepares from its excess blood is therefore never more than 14 days old and usually less. From this it follows that the electrolyte, protein and other constituents of the plasma are well within the acceptable limits for transfusion and the vacuum packing of the lyophilized product ensures stability for many years. The bloods selected for plasma are mostly group A and B, low in titre of iso-agglutinins and haemolysin-free. The anti-

en plasma normaalweg gebruik sou word.

Dit strek tot eer van die fabrikante van hierdie plasma-plaasvervangers dat hulle nooit aanspraak daarop gemaak het dat hul produkte uit 'n chemiese of fisiologiese oogpunt die gelyke van menslike plasma was nie.

In ons korrespondensiekolomme in hierdie uitgawe oefen dr. S. Rainsford kritiek op ons inleidingsartikel van 23 November 1957 uit. Dit is duidelik dat hy hom ten doel stel om te bewys dat dekstran nie alleen net so goed soos plasma is nie, maar in sommige opsigte selfs beter. Waar hy dit probeer doen, gaan hy heelwat verder as enige lewende gesaghebbende op hierdie besondere gebied, en dit is derhalwe nodig om sy aansprake en sy kritiek te evalueer.

In die eerste plaas moet daar beklemtoon word dat ons Inleidingsartikel bedoel was om die belangrike aankondiging dat bloedplasma nou vryelik deur die Suid-Afrikaanse Bloedoortappingsdiens tot beskikking van praktisyns dwarsdeur die Unie gestel word, te onderstreep. Niks wat in daardie Inleidingsartikel voorgekom het, kan as afkammende kritiek beskou word op die gebruik van plasma-plaasvervangers in noodtoestande soos oorlog, of selfs in die private burgelike praktyk waar menslike bloed en plasma miskien nie beskikbaar is of nie in voldoende hoeveelhede verkry kan word nie. Die punt is egter benadruk dat geeneen van die sogenaamde plasma-plaasvervangers wat tot dusver verkrygbaar is, as doeltreffend beskou kon word nie, en, om ons bewering te staaf, is die gewigtige mening van die skrywers van *Dextran, Its Properties and Use in Medicine* aangehaal. 'n Verdere aanhaling uit dieselfde werk (op bl. 7) behoort die wettige rol van ‚plasma-bespaarders' in die mediese praktyk te verduidelik.

‚Dekstranoplossings en ander plasma-plaasvervangers speel waarskynlik hul grootste rol (1) in die normale oortappingspraktyk onderwyl daar op verenigbaarheidstoetse gewag word, en *wanneer plasma nie beskikbaar is nie* (ons kursivering), (2) op plekke waar daar om klimaats-, aardrykskundige of finansiële redes geen doeltreffende oortappingsdienste bestaan nie, en (3) in landswye noodgevalle.'

Ons het ook verklaar dat die plasma wat tans in Suid-Afrika beskikbaar gestel word, op 'n eenheid-vir-eenheid grondslag voorberei word van die ‚surplus van ongebruikte bloed' d.w.s. van bloed wat die onmiddellike behoeftes oorskry, en nie van ‚tyd-verstreke bloed' nie. Die bruikbaarheidstydperk van heelbloed in 'n suursitraat-dekstrose-oplossing word gewoonlik op drie weke vasgestel; op baie plekke word dit selfs tot 4 weke verleng. Om te verseker dat bloed so vars as moontlik gebruik word, is die bruikbaarsheidstydperk by die Suid-Afrikaanse Bloedoortappingsdiens tot 2 weke verminder.

coagulant employed per 500 c.c. of whole blood is 75 c.c. of a 2.14% solution of sodium citrate, 0.8% citric acid and 2.23% glucose. On reconstitution of the lyophilized plasma with distilled water, the pH is 7.4. Dr. Rainsford's statement that 'it is heavily diluted with acid citrate dextrose, usually to the extent of 100 c.c. to every 150 c.c. of plasma', is therefore inapplicable in the case of the plasma to which our Editorial referred, as is also his statement that 'it is a highly acid solution whose buffering capacity is not all that good'.

The most important haemostatic factor contained in plasma is fibrinogen and this factor is remarkably stable. In fact, all commercially produced fibrinogen presently available in South Africa is prepared from *outdated pooled plasma.* Dr. Rainsford's statement that 'because of the excess of citrate in such plasma, it can and does sometimes exert precisely the reverse effect' is at variance with clinical experience. Indeed, the transfusion of whole blood with or without plasma is standard treatment in all haemorrhagic states, as he himself admits. Significantly, he has omitted to state that dextran itself has a known heparin-like effect and 'has been shown to cause a defect in the haemostatic mechanism in normal individuals' (*Dextran,* by Squire *et al.,* at p. 53).

Furthermore, Langdell *et al.* recently concluded, in a paper published on 25 January 1958 and entitled *Dextran and Prolonged Bleeding Time*: *

'The infusion of 1,000 ml. of commercially available dextran solution into normal adult humans resulted in a hemostatic defect characterized by a prolonged bleeding time. In 8% of the subjects the bleeding time after dextran exceeded 30 minutes. The maximum incidence did not occur immediately after the infusion but three to nine hours later. . . . The mode of action is not clear, but the phenomenon appears to be due to interference with platelet activity. Dextran infusion would appear to be contraindicated in patients with a known bleeding tendency or to whom large transfusions of whole blood have been given. The use of large infusions of dextran alone also carries a risk of serious failure of the hemostatic mechanism.'

The diminution of the risk of transmission of virus hepatitis by the preparation of plasma on a unit-for-unit basis is a matter of simple arithmetic. By definition, the risk of transmission per unit of plasma cannot be higher than from the whole blood from which each unit of plasma is derived. As with whole blood, this risk of infection—such as it is—is multiplied according to the number of units of plasma employed. In pooled plasma, on the other hand, the risk per unit is the same as

* Langdell *et al.* (1958): J. Amer. Med. Assoc., **166,** 346.

Die plasma wat die Diens van sy oortollige bloed voorberei, is derhalwe nooit ouer as veertien dae nie. In die reël is dit gewoonlik minder. Hieruit volg dat die elektrolitiese, proteïen- en ander bestanddele van die plasma altyd goed binne die aanneemlike grense vir oortapping is, en die lugdigte verpakking van die geliofiliseerde produk verseker stabiliteit oor 'n tydperk van baie jare. Die bloedsoorte wat vir plasma uitgesoek word, behoort meestal aan Groep A en B, laag in titer van iso-agglutiniene en hemolisien-vry. Die stollingsbestrydingsmiddel wat per 500 k.s. heelbloed gebruik word, is 75 k.s. van 'n 2.14% oplossing van natriumsitraat, 0.8% sitroensuur en 2.3% glukose. By hersamestelling van die geliofiliseerde plasma met gedistilleerde water is die pH 7.4. Dr. Rainsford se verklaring dat ‚dit erg verdun word met suur-sitraat-dekstrose, gewoonlik tot die omvang van 100 k.s. vir iedere 150 k.s. plasma,' is derhalwe nie van toepassing op die plasma waarna in ons Inleidingsartikel verwys word nie. Dit geld ook vir sy verklaring dat ‚dit 'n baie suur oplossing is, die buffervermoë waarvan veel te wense oorlaat.'

Die belangrikste hemostatiese faktor wat in plasma voorkom, is fibrinogeen, en die faktor is merkwaardig stabiel. Inderdaad, al die kommersieel geproduseerde fibrinogeen wat tans in Suid-Afrika verkrygbaar is, is voorberei van *verouderde saamgevoegde plasma.* Dr. Rainsford se verklaring dat ‚weens die oormaat van sitraat in sodanige plasma dit presies die teenoorgestelde effek kan uitoefen. en dit inderdaad ook soms doen,' is in stryd met kliniese ondervinding. Trouens, die oortapping van heelbloed met of sonder plasma is standaard-behandeling in alle hemorragiese gevalle, soos hy self erken. Dit is betekenisvol dat hy nalaat om te sê dat dekstran self 'n bekende heparienagtige effek het, en ‚dat daar reeds aangetoon is dat dit die oorsaak was van 'n defek in die hemostatiese meganisme van die normale individu.' (*Dextran* deur Squire, *et al.,* op bl. 53).

Temeer, in 'n referaat wat op 25 Januarie 1958 gepubliseer en *Dextran and Prolonged Bleeding Time* getiteld is, het Langdell *et al.* tot die volgende slotsom geraak: *

‚Die infusie van 1,000 ml. van kommersieel beskikbare dekstran in normale, volgroeide mense het 'n hemostatiese effek, gekenmerk deur 'n langdurige bloedingstyd, tot gevolg gehad. By 8% van die pasiënte het die bloedingstyd ná behandeling met dekstran 30 minute oorskry. Die maksimum-voorkomssyfer is waargeneem nie onmiddellik na die infusie nie, maar wel drie tot nege uur later. . . . Die werkingsmetode is nie heeltemal duidelik nie, maar dit wil voorkom asof die verskynsel te wyte is aan 'n versteuring van die plaatjie-aktiwiteit. Dit skyn asof daar kontraindikasies vir dekstran-infusie is by pasiënte met 'n bekende neiging tot bloeding of wat reeds oortappings met groot hoeveelhede heelbloed ontvang het. Die gebruik van groot infusies van dekstran alleen bring ook die gevaar van 'n ernstige versaking van die hemostatiese meganisme mee.'

Die vermindering van die gevaar van die oordrag van virus-lewerontsteking deur die voorbereiding van plasma op 'n eenheid-vir-eenheid-grondslag is 'n saak

* Langdell *et al.* (1958): J. Amer. Med. Assoc., **166,** 346.

that from the pool from which it is derived. It needs only one infected plasma to contaminate the entire pool. Our Editorial did not claim that the risk of transmission of hepatitis had been completely eliminated. We stated that this risk was negligible. No case of hepatitis due to the infusion of single-unit plasma has, in fact, so far been reported in South Africa.

Admittedly, the preparation of plasma on a unit-for-unit basis with individual bacteriological controls is expensive, but that is hardly a scientific argument against its use. In this connexion, the cost of plasma in South Africa is at present £3 per unit to the private patient and £2 15s. to hospitals—a price which compares very favourably indeed with the price of plasma produced anywhere in the world. The method of processing (using sterile, pyrogen-free disposable equipment throughout) eliminates the necessity for bacterial filtration or pyrogen testing. Such febrile and allergic reactions as do occur are at least as uncommon as with dextran which, as is well known, may itself cause antigenic reactions.†

We are in agreement with Dr. Rainsford's contention that dextran should be stockpiled for the possible contingency of thermo-nuclear warfare; but so also should plasma, for which there will be an even greater need.

The clear implication of Dr. Rainsford's argument is that the use of dextran in preference to plasma should be encouraged in civilian practice 'so as to ensure that the medical and nursing professions will be fully conversant with its clinical applications'. This is an odd argument indeed. If dextran is, in fact, as innocuous as Dr. Rainsford believes, peacetime practice in its use is surely unnecessary, particularly since dextran can be administered with the same facility as a saline solution, whereas reconstitution of lyophilized plasma with the diluent does require some familiarity with the technique.

The duty of the doctor is to do the best for his patient under all conditions and it seems to us obvious that if plasma is indicated and available it should be used in preference to so-called plasma substitutes. In a paper on *Shock* in the series *Emergencies in General Practice*, Sir Heneage Ogilvie* very aptly referred to the role of 'plasma savers' as follows:

'What is their place in the treatment of shock? The answer is in the seventh chapter of St. Matthew's Gospel: "What man is there of you, whom if his son ask bread, will give him a stone?"'

* Ogilvie, H. (1955): Brit. Med. J., **1**, 159.
† Kabat, E. A. and Berg, D. (1953): *Dextran-Antigen in Man*, J. Immunol., **70**, 514.

van eenvoudige rekenkunde. Logies kan die oordraggevaar per eenheid plasma nie hoër wees as die gevaar verbonde aan die heelbloed waarvan iedere eenheid plasma voorberei word nie. Net socs in die geval van heelbloed word hierdie infeksie-gevaar—in die mate waarin dit wel bestaan—vermenigvuldig ooreenkomstig die aantal eenhede plasma wat gebruik word. In die geval van saamgevoegde plasma, daarenteen, is die gevaar per eenheid dieselfde as die gevaar opgelewer deur die samevoeging waarvan dit voorberei word, en slegs een besmette plasma is nodig om die hele samevoeging te besmet. In ons Inleidingsartikel het ons nie aanspraak daarop gemaak dat die gevaar van die oordrag van lewerontsteking heeltemal uitgeskakel is nie. Ons het gesê dat hierdie gevaar onbenullig is. Geen geval van lewerontsteking volgende op die oortapping van 'n enkele-eenheid plasma is inderdaad tot dusver in Suid-Afrika gerapporteer nie.

Ons erken dat die voorbereiding van plasma op 'n eenheid-vir-eenheid-grondslag met individuele bakteriologiese kontroles 'n duur onderneming is, maar dit vorm nie juis 'n wetenskaplike argument teen die gebruik daarvan nie. In hierdie verband kan ons miskien sê dat die prys van plasma in Suid-Afrika op die oomblik £3 per eenheid vir die private pasiënt en £2 15s. vir hospitale is. Dit vergelyk baie gunstig met die prys van plasma elders in die wêreld. Die bewerkingsmetode en die gebruik deurgaans van steriele, pirogeenvrye toerusting wat daarna vernietig word, maak bakteriese filtrasie of pirogeentoetse heeltemal onnodig. Die koorsige en allergiese reaksies wat wel voorkom, is ten minste net so seldsaam as wanneer daar gebruik gemaak word van dekstran wat, soos goed bekend is, self antigeniese reaksies tot gevolg kan hê.†

Ons stem saam met dr. Rainsford se bewering dat voorrade dekstran opgebou moet word vir moontlike noodgevalle as 'n termo-nukleêre oorlog uitbreek. Maar dit geld ook vir plasma waaraan daar 'n selfs groter behoefte sal ontstaan.

Die duidelike implikasies van dr. Rainsford se argument is dat die gebruik van dekstran liewer as plasma aangemoedig behoort te word in die burgerlike praktyk ‚om te verseker dat die mediese en verpleegprofessies volkome op hoogte van die kliniese toepassings daarvan sal wees.' Dit is 'n sonderlinge argument. Indien dekstran inderdaad so onskadelik is soos dr. Rainsford skynbaar glo, is die vredestydse beoefening van die gebruik daarvan tog seker onnodig, veral met die oog op die feit dat dekstran net so maklik soos 'n soutoplossing toegedien kan word. Daareenteen vereis die hersamestelling van geliofiliseerde plasma met die oplosmiddel 'n sekere mate van kennis van die tegniek.

Dit is die plig van die dokter om in alle omstandighede die beste vir sy pasiënt te doen, en vir ons skyn dit vanselfsprekend te wees dat as plasma aangedui word en beskikbaar is, dit gebruik moet word liewer as die sogenaamde plasma-plaasvervangers. In 'n referaat oor *Skok* in die reeks *Emergencies in General Practice*, verwys sir Heneage Ogilvie* op 'n treffende manier na die rol van ‚plasma-bespaarders'. Hy sê:

‚Watter rol speel hulle in die behandeling van skok? Die antwoord word gevind in die sewende hoofstuk van die Evangelie volgens Matteus: „Of watter mens is daar onder julle wat, as sy seun hom brood vra, vir hom 'n klip sal gee?"'

* Ogilvie, H. (1955): Brit. Med. J., **1**, 159.
† Kabat, E. A. en Berg, D. (1953): *Dextran-Antigen in Man*, J. Immunol., **70**, 514.

REVIEWS OF BOOKS

ENDOCRINOLOGY OF BREAST CANCER

Endocrine Aspects of Breast Cancer. Edited by Alastair R. Currie, B.Sc., M.B., F.R.C.P.Ed. 1958. (Pp. 330 + Index. With Figs. 37s. 6d.). Edinburgh and London: E. & S. Livingstone Ltd.

In July 1957 a Conference, under the auspices of the University of Glasgow, was held in the Western Infirmary and the Royal Infirmary. The participants included outstanding names in the field of breast cancer.

Eminent endocrinologists also contributed to the discussions.

The *Proceedings* of the Conference have now been published under the editorship of Dr. Alastair R. Currie.

This is a most important monograph, which touches on the day-to-day activities, not only of specialists, but also of general practitioners.

The modern management of breast cancer overrides treatment confined to local surgery. Paradoxically, endocrines may be used both by techniques of subtraction and addition. An important discussion ranged over the respective merits of removal of the ovaries and the adrenals as against extirpation of the pituitary, whether the latter was done surgically or by implantation with radio-active isotopes. Atkins (of Guy's Hospital, London) concluded that in hypophysectomy 'we have a therapeutic measure which is almost certainly as good as, and may be better than, adrenalectomy with oophorectomy' (p. 73).

South African readers will be particularly interested in the technique of pituitary destruction by irradiation, because of the important contribution made in this country recently by Weinbren, Jackson and Gamsu, whose paper entitled *Implantation of Radon Seeds into the Pituitary Fossa in the Treatment of Secondary Deposits from Cancer of the Breast* appeared in this Journal last year (Vol. 3, No. 11, at p. 249).

The probably pre-eminent role of the pituitary hormone prolactin was high-lighted during the more purely endocrine sessions of the meeting and attention was drawn to the preference that should possibly be given to pituitary ablation. Attention was also drawn to the fact that theorectically pituitary ablation would seem preferable 'by reason of its double effect, both directly through mammotrophin and somatotrophin and indirectly through adrenal and ovarian suppression. But cortisone withdrawal studies show that, even after complete hypophysectomy, the adrenals may exhibit some small activity and therefore presumably may secrete oestrogens; moreover, clinical observations indicate that hypophysectomy is not usually complete. Thus neither adrenalectomy nor hypophysectomy alone can meet all the indications. Atkins' studies indicate that the clinical results of the two types of procedure do not differ very greatly. Perhaps, as Boyland suggests, we should be more willing to undertake both. Although Loraine's gonadotrophic findings offer support for the view that there are differences in hormonal status between patients with responsive tumours and resistant ones, our discussions confirmed the general impression that we still lack criteria on which to base our selection of cases for treatment, for the responsive tumour appears to have no characteristic histological picture and no feature in the clinical picture is significant. Cade's figures suggest that deterioration following androgen or oestrogen administration, or improvement after prednisone, may give some indication of hormone dependence, and Jessiman's results on calcium excretion after oestrogens may also be helpful, but it still remains true that the result of operation can only be decided by trial.'

No practitioner, actively concerned with the problems of diagnonsis, treatment and after-care of breast cancer, should neglect to study closely this readable and authoritative review of one of the most urgent problems in medical practice.

INSECTICIDES

Expert Committee on Insecticides, Seventh Report. World Health Organization. Technical Reports Series, 1957, No. 125; Pp. 31. 1s. 9d. Pretoria: Van Schaik's Bookstore (Pty.) Ltd., P.O. Box 724.

The diseases transmitted by arthropods, particularly the insect-borne diseases, constitute one of the most important problems with which national health administrations are confronted. The initial results obtained with modern insecticides gave rise to the hope that most of these diseases could be successfully controlled, even completely eradicated, within a short period. However, the resistance to chlorinated hydrocarbon insecticides which has appeared in various vector species, has changed this outlook. Resistance, which has developed much more rapidly than the measures available to combat it, is now the main obstacle in the fight against arthropod-borne diseases; so the Expert Committee on Insecticides devoted its 7th session more particularly to a study of the problem of resistance and to the international measures called for.

The *Report* stresses that resistance is now universal in the house fly, that it is frequently found in the louse and that it has been reported in various species of mosquito (*Anopheles, Aëdes aegypti, Culex*) as well as in at least 27 other insect species. A WHO inquiry to determine what research is under way on the resistance problem has shown the inadequacy of the work in this field. The *Report* indicates the broad outline of an international coordinated research programme on resistance, which should include, in particular, the collection and diffusion of information, the promotion of research, the increase of personnel and financial means devoted to this work, the adoption of standard test methods, the testing of new insecticides, the establishment of satisfactory liaison between research workers and laboratories, and the convening of meetings and conferences.

The *Report* adopts, with certain amendments, the definition of resistance formulated during the *Symposium on the Control of Insect Vectors of Disease* (Rome, 1953) and recommends means to detect and measure resistance. It discusses the various applications of a standard test method, which would make it possible to obtain data on the appearance of resistant insect strains. It also mentions certain problems connected with the biological aspects of resistance, which should be studied without delay.

A second part of the *Report* on the disinsectization of aircraft contains revised specifications for aerosols and aerosol dispensers accompanied by a description of suitable test methods, as well as new recommendations for quarantine disinsectization.

FIRST SOUTH AFRICAN MEDICO-LEGAL CONGRESS

The South African Medico-Legal Society has arranged for this Congress to be held in Johannesburg, from Thursday night 31 July to Saturday mid-day, 2 August 1958. The exact venue of the meeting will be announced later.

The following topics are provisionally scheduled for discussion:

1. *Artificial Insemination.*
2. *A Symposium on Acute Alcoholism.*
3. *Problems of Blood Transfusion.*
4. *A Symposium on Sudden Death in Infancy.*
5. *Problems of Consent to Medical Procedures.*
6. *Two Recent American Films* (in sound) entitled *The Medical Witness* and *The Doctor Defendant* will be screened, followed by a discussion on the films, and an *Open Forum* on any topic discussed at the Congress.

These films have been sponsored by the Wm. S. Merrell Company of Cincinnati, in co-operation with the American Medical Association and the American Bar Association. The Wm. S. Merrell Company has kindly made the films available for this Congress.

7. *Medico-Legal Exhibits and a Visit to the South African Blood Transfusion Centre.*

The Congress registration fee for members of the South African Medico-Legal Society is 10s. 0d. The registration fee for non-members is £1 10s. 0d. (The normal subscription for membership of the South African Medico-Legal Society is £2 2s. 0d. This includes a free subscription to the *Journal of Forensic Medicine.*)

Colleagues who wish to register for attendance at this Congress must advise the Honorary Organizing Secretary not later than 30 June 1958. This will enable adequate accommodation arrangements to be made for the meetings and ensure sufficient time for the printing of a Congress prospectus which, it is hoped, will include the names and addresses of all participants in the Congress.

All communications must be directed to:

Honorary Organizing Secretary (Dr. H. A. Shapiro), First South African Medico-Legal Congress, P.O. Box 1010, Johannesburg.

EERSTE SUID-AFRIKAANSE MEDIES-GEREGTELIKE KONGRES

Die Suid-Afrikaanse Medies-Geregtelike Vereniging het gereël dat hierdie Kongres vanaf Donderdagaand, 31 Julie, tot 12-uur middag op Saterdag, 2 Augustus 1958, gehou sal word. Die plek van byeenkoms sal later aangekondig word.

Daar is voorlopig bepaal dat die volgende onderwerpe bespreek sal word:

1. *Kunsmatige Inseminasie.*
2. *'n Simposium oor Akute Alkoholisme.*
3. *Probleme Opgelewer deur Bloedoortapping.*
4. *'n Simposium oor Skielike Sterfgevalle tydens die Suigelingsjare.*
5. *Probleme Opgelewer deur die Toestemming wat vir Mediese Prosedures Nodig is.*
6. *Twee Onlangse Amerikaanse Klankrolprente* getiteld *The Medical Witness* en *The Doctor Defendant* sal vertoon word, gevolg deur 'n bespreking van die rolprente, en 'n *Oop Forum* oor enige onderwerp wat tydens die Kongress te berde gebring is.

Die Wm. S. Merrell Company, van Cincinnati, in medewerking met die Amerikaanse Geneeskundige Vereniging en die Amerikaanse Regsvereniging, was verantwoordelik vir die produksie van hierdie rolprente, en die Wm. S. Merrell Company het hulle goedgunstiglik tot beskikking van die Kongres gestel.

7. *Medies-Geregtelike Uitstallings en 'n Besoek aan die Suid-Afrikaanse Bloedoortappingsdiens.*

Die Kongres-registrasiegeld vir lede van die Suid-Afrikaanse Medies-Geregtelike Vereniging is 10s. 0d. Die registrasiegeld vir nie-lede is £1 10s. 0d. (Die normale ledegelde van die Suid-Afrikaanse Medies-Geregtelike Vereniging is £2 2s. 0d. Dit sluit in *gratis* intekengeld op die *Journal of Forensic Medicine.*)

Kollegas wat hierdie Kongres wil bywoon en hulle wil laat registreer, moet die organiserende Ere-sekretaris voor 30 Junie 1958 in kennis stel. Dit sal dit moontlik maak om doeltreffende akkommodasiereëlings vir die vergaderings te tref, en voldoende tyd laat vir die druk van 'n Kongresprospektus wat, na gehoop word, die name en adresse van alle deelnemers aan die Kongres sal insluit.

Alle briewe moet gerig word aan:

Die Organiserende Ere-Sekretaris (Dr. H. A. Shapiro), Eerste Suid-Afrikaanse Medies-Geregtelike Kongres, Posbus 1010, Johannesburg.

TUBELESS DETECTION OF GASTRIC ACIDITY

Knowledge of the degree of gastric acidity has provided substantial aid in the diagnosis of duodenal ulcer, gastric cancer and pernicious anaemia.

'The claim that gastric cancer occurs three times more frequently in achlorhydrics than in persons secreting hydrochloric acid, and ten times more frequently in achylic individuals over 40 years of age, has stressed the value of screening individuals for further diagnostic procedures aimed at the early detection of gastric cancer. In the presence of a gastric ulcer niche or of anaemia, the knowledge of the status of gastric acidity may provide a basis for further therapeutic and diagnostic procedures. The estimation of gastric acidity in a subtotal gastrectomized patient may be a contributing factor in the diagnosis of a marginal ulcer. In the absence of demonstrable organic disease the lack of free gastric acid may be a useful guide in prescribing substitution therapy.

'In the past, the failure to ascertain by intubation the state of gastric acidity in a specific case or in a mass screening project could have been justified by pleading inconvenience or impracticability. The advent of tubeless gastric analysis makes these reasons for omission no longer acceptable'.[1]

Segal, Miller and Morton introduced the first practical technique for estimating gastric acidity by a tubeless method of gastric analysis. The tubeless technique has since been further simplified by the development of a new dye compound containing Azure A as the indicator dye. This makes it possible to determine the presence or absence of free hydrochloric acid in the stomach by merely appraising, naked-eye, a blue colour change in the urine

RATIONALE OF THE TEST

The Azure A dye is released from its complex in the presence of free hydrochloric acid, is absorbed in the small gut and is then excreted in the urine, where it can be detected by a colour change. In the absence of free hydrochloric acid in the stomach, the dye compound passes intact into the small bowel and very

1. Segal, H. L., Miller, L. L. and Morton, J. J. (1957): *Monographs on Therapy: Diagnex Blue in the Determination of Gastric Acidity*, **2**, 147.

BUISLOSE OPSPORING VAN MAAGSURIGHEID

Kennis van die mate van maagsurigheid help aansienlik met die diagnose van duodenale swere, maagkanker en kwaadwillige bloedarmoede.

'Die bewering dat maagkanker drie keer meer dikwels by achloorhidrie-lyers voorkom as by persone wat soutsuur afskei, en tien keer meer dikwels by achylia-lyers bo die ouderdom van veertig jaar, beklemtoon die waarde van die ondersoek van individue vir verdere diagnostiese prosedures wat op die vroeë ontdekking van maagkanker toegespits is. In die aanwesigheid van 'n maagsweer-nis of van bloedarmoede kan 'n kennis van die status van maagsurigheid 'n grondslag vir verdere terapeutiese en diagnostiese prosedures verskaf. Die vasstelling van maagsurigheid in 'n subtotale gastrektomiepasiënt kan 'n bydraende faktor wees in die diagnose van 'n marginale sweer. In die afwesigheid van bewysbare organiese siekte kan die gebrek aan vrye maagsuur 'n nuttige gids by die voorskrywing van substitusie-terapie wees.

Die versuim in die verlede om die toestand van maagsurigheid deur middel van intubasie vas te stel by 'n spesifieke geval of in 'n grootskeepse ondersoekskema kon miskien geregverdig geword het deur te wys op die ongerief of die praktiese onuitvoerbaarheid van intubasie. Met die koms van buislose maagontleding is hierdie redes egter nie langer aanneemlik nie'.[1]

Segal, Miller en Morton was die eerste wat 'n praktiese tegniek vir die vasstelling van maagsurigheid deur 'n buislose metode van maagontleding beskikbaar gestel het. Die buislose tegniek is sedertdien verder vereenvoudig deur die ontwikkeling van 'n nuwe verfstofsamestelling wat Asuur A as die indikatorverfstof bevat. Dit maak dit moontlik om die aan- of afwesigheid van vrye soutsuur in die maag vas te stel deur bloot 'n blou kleurverandering in die urine met die blote oog te betrag.

DIE RASIONELE BASIS VAN DIE TOETS

Die Asuur A-verfstof word uit sy samestelling vrygestel in die aanwesigheid van vrye soutsuur. Dit word dan in die dunderm geabsorbeer en saam met die urine afgeskei waar dit deur 'n kleurverandering aangedui word. In die afwesigheid van vrye soutsuur in die maag gaan die verfstofsamestelling ongeskonde na die dunderm, en baie min van die Asuur A word dan binne die eersvolgende 2 uur saam met die urine afgeskei.

1. Segal, H. L., Miller, L. L. en Morton, J. J. (1957): *Monographs on Therapy: Diagnex Blue in the Determination of Gastric Acidity*, **2**, 147.

little of the Azure A is then excreted in the urine within the next 2 hours.

The chain of events necessary for the proper execution of this test must not be interfered with, e.g.:

'Vomiting will prevent proper ion exchange in the stomach and pyloric obstruction will decrease the availability of the dye for absorption in the small intestinal tract. Severe malabsorption, marked cardiac failure or dysfunction of the liver or kidneys or urinary retention likewise will distort the accuracy of the test by interfering with the normal urinary excretion range of the Azure A dye'.[1]

No unpleasant side effects or toxic reactions occurred in any of more than 1,500 persons tested with the Azure A complex.

The consensus of clinical opinion indicates that, when properly used, the Azure A complex provides a reliable, simple and tubeless way of detecting achlorhydria by the simple appraisal of a colour change in the urine. It appears to be a reliable clinical method of differentiating between the presence or absence of free hydrochloric acid. The results of the tubeless test may be more accurate than those obtained by intubation in determining the presence or absence of free gastric acid because the mere act of introducing the tube inhibits gastric secretion in some patients.

THE SIMPLICITY OF THE PROCEDURE

Many of the problems of intubation are eliminated and the test may obviously be applied to large groups of persons with a minimum of technical failure. Silon *et al.*[2] comment that it is probably the most practical method yet devised for determining gastric acidity by a tubeless method.

It is clearly of particular value in a gastric cancer detection campaign for screening achlorhydric and hypochlorhydric subjects among whom the incidence of cancer of the stomach is higher than would be expected in a similar age group in the general population.[3] Likely candidates selected by the tubeless technique can then be subjected to more detailed studies, repeated at intervals, if necessary, to detect early asymptomatic gastric cancer.

2. Silon, N., Olson, K. B. and Gillie, E. (1957): *Monographs on Therapy: Dignex Blue in the Determination of Gastric Acidity*, **2**, 166.
3. Fentress, V. and Sandweiss, D. J. (1957): *Monographs on Therapy: Diagnex Blue in the Determination of Gastric Acidity*, **2**, 168.

Die reeks voorvalle wat nodig is vir die behoorlike uitvoering van hierdie toets moet nie versteur word nie, bv.:

‚Braking sal behoorlike ioon-wisseling in die maag voorkom, en maaguitgangobstruksie verminder die beskikbaarheid van die verfstof vir absorpsie in die dundermkanaal. Ernstige wanabsorpsie, opvallende hartversaking of disfunksie van die lewer of die niere, of urinebehoud sal ook die akkuraatheid van die toets versteur deur die normale urine-afskeidingsbestek van die Asuur A-verfstof in die wiele te ry'.[2]

Geen onaangename newe-effekte of toksiese reaksies is waargeneem by die meer as 1,500 persone wat met die Asuur A-kompleks behandel is nie.

Allerweë word daar in kliniese kringe gemeen dat as die Asuur A-kompleks behoorlik gebruik word, dit 'n betroubare, eenvoudige en buislose manier is om achloorhidrie vas te stel deur die eenvoudige betragting van 'n kleurverandering in die urine. Dit skyn asof dit 'n betroubare kliniese metode is om te onderskei tussen die aanwesigheid of afwesigheid van vrye soutsuur. Die resultate van die buislose toets kan inderdaad betroubaarder wees as dié wat met intubasie verkry word wanneer die aanwesigheid of afwesigheid van vrye maagsuur vasgestel moet word, want die blote introduksie van 'n buis strem maagafskeidings by sommige pasiënte.

DIE EENVOUDIGHEID VAN DIE PROSEDURE

Baie van die probleme van intubasie word uitgeskakel, en dis duidelik dat die toets op groot groepe persone toegepas kan word met minimale tegniese vergissings. Silon *et al.*[2] meen dat dit die mees praktiese metode is wat tot dusver ontwerp is vir die vasstelling van maagsurigheid volgens die buislose metode.

Dit is duidelik dat dit van besondere waarde gaan wees in die veldtog vir die ontdekking van maagkanker. Hierdie veldtog vereis die ondersoek van 'n groot aantal achloorhidrie- en hipochloorhidrie-pasiënte by wie maagkanker meer dikwels voorkom as wat 'n mens sou verwag by 'n dergelike ouderdomsgroep uit die algemene bevolking.[3] Waarskynlike kandidate wat deur die buislose tegniek aangewys word, kan dan onderwerp word aan breedvoeriger studies wat, indien nodig, by tussenpose herhaal kan word om vroeë asimptomatiese maagkanker op te spoor.

2. Silon, N., Olson, K. B. en Gillie, E. (1957): *Monographs on Therapy: Diagnex Blue in the Determination of Gastric Acidity*, **2**, 166.
3. Fentress, V. en Sandweiss, D. J. (1957): *Monographs on Therapy: Diagnex Blue in the Determination of Gastric Acidity*, **2**, 168.

CLINICAL STUDIES ON TRAL WITH PHENOBARBITAL

HEXOCYCLIUM, ABBOTT

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Pharmacology. Tral is a new quaternary ammonium salt with a post-ganglionic blocking effect. It has the chemical name N–(B – cyclohexyl – B – hydroxy – B – phenylethyl) –N'–methylpiperazine methosulfate.

Tral with phenobarbital was used in these clinical trials, 25 mg. with 15 mg. phenobarbital administered orally 4 times daily, one tablet before each meal and one on retiring.

The pharmacology of Tral revealed it to be a potent and specific post-ganglionic anti-chlonergic or anti-muscarinic drug. It was demonstrated on animals that the drug possessed a gastric anti-secretory effect.

Its anti-spasmodic potency against acetylcholine-induced spasm of isolated rabbit ileum is slightly weaker than that of atropine.

The anti-motility effect of Tral in the unanaesthetized dog is comparable to that of atropine.

Toxicity. Animal studies reveal that Tral has a wide margin of safety in the recommended dose.

CLINICAL TRIALS

The purpose of these clinical trials was to ascertain the effects of Tral plus Phenobarbitone in cases of acute ulceration in the stomach and duodenum. A further observation was the assessment of the side effects of the drug. All cases chosen for treatment with Tral were, at the time of the trials, in an acute stage of the disease, i.e. they were suffering from active symptoms.

A second group of patients was chosen in which the diagnosis of irritable colon was established; after all other conditions had been excluded. The experiment was based purely on the clinical response to the drug. No assessment by means of gastric analysis, radiological study or any other form of laboratory investigation was undertaken.

PEPTIC ULCER

In this group 29 patients suffering from peptic ulcer, both gastric and duodenal, were treated with Tral with Phenobarbitone. The dosage was standardized in all cases; one tablet was given before each meal and one on retiring. All patients were ambulatory. There was no restriction of diet, alcohol or tobacco. All forms of medicaments were withdrawn while the patients were on Tral. In all these cases abdominal pain was the main feature.

The patients were observed for the symptomatic relief of pain, the time interval before such relief was obtained and the duration of remission from pain. The effect on other symptoms such as nausea, vomiting, pyrosis, hunger and anorexia, were also noted.

There were 6 cases of gastric ulcer and 23 cases of duodenal ulcer treated with Tral and Phenobarbitone, all patients receiving the same dosage.

Pain was relieved completely in 27 patients. The two cases which failed to respond to treatment were both cases of gastric ulcer lying posteriorly near the gastro-oesophageal junction. In these two cases there was no relief of pain at all. The patients who were relieved of pain were free of this symptom within a period of 1–5 days. Three cases of duodenal ulcer had relief on the first day of treatment. Eight cases of duodenal ulcer were relieved on the second day of treatment. Three cases of duodenal ulcer and three cases of gastric ulcer were relieved on the third day of treatment. Nine cases of duodenal ulcer were relieved on the fourth day of treatment. One case of gastric ulcer was relieved on the fifth day of treatment. The degree of relief of pain continued to increase progressively each day. By the end of the tenth day all patients were completely free of pain. All patients continued on treatment for eight weeks. During this period they were completely free of symptoms. In none of the cases was there any evidence of the symptoms of nausea, vomiting, pyrosis, hunger or anorexia.

Side Effects. In all patients treated the side effects were very minimal. Six complained of dryness of the mouth, but this did not disturb any of these patients. There was no disturbance of vision or micturition in the cases studied. Ten of the patients had been treated with other anti-cholinergics. These patients were able to compare the side effects of Tral

with those of the other drugs. All patients stated that the side effects (drying of the mouth, etc.) were far less severe than those of other anti-cholinergics.

IRRITABLE COLON

Nine cases of irritable colon were studied. In all these cases the diagnosis was arrived at by exclusion of organic disease of the bowel and by the typical symptomatology of this disease.

In these cases the relief of symptoms of abdominal pain, abdominal distension and constipation and diarrhoea were noted. In 7 cases there was a marked improvement in the symptoms; 2 cases experienced partial relief.

The rapidity of the onset of relief was more prolonged than that of the peptic ulcer group. On the average, improvement of symptoms occurred from the seventh day to the twelfth day. All these patients were chronic sufferers from the disease and had not previously obtained any form of relief.

The relief of symptoms persisted while the patients were on the drug, the treatment continuing for a period of 12 weeks. During this time all were greatly relieved. On withdrawal of the drug, the symptoms reappeared in a short time in 7 of the cases. The treatment was continued at the request of the patients, with immediate relief of symptoms. They have continued the use of Tral daily and remain free of symptoms.

CONCLUSIONS

Tral is effective for the treatment of peptic ulcer and irritable colon. It is fully realized that in both these conditions there may be a psychogenic response to any new form of therapy. It is also realized that Phenobarbitone in itself can produce relief of these conditions. However, as the response to treatment was uniform in all these cases, there is a suggestion that the drug was effective through its pharmacological action and it is unlikely that the relief obtained was psychological. Cases treated purely with Phenobarbitone do not show the same prompt response and, therefore, one can conclude that it is unlikely that Phenobarbitone itself was responsible for the relief of symptoms.

It would seem that Tral is a suitable therapeutic agent for the treatment of peptic ulcer and irritable colon. It is particularly effective because of the minimal side effects produced. In comparison with other anticholinergics, the drug appears to have a much wider response, particularly in the irritable colon group.

OPSOMMING

Tral is doeltreffend vir die behandeling van peptiese swere en 'n geprikkelde kolon. Daar word ten volle besef dat daar in albei toestande 'n psigogeniese reaksie op enige nuwe vorm van terapie kan wees. Daar word ook besef dat fenobarbitoon op sigself verligting van hierdie toestande kan meebring. Hoe dit ook al sy, aangesien die reaksie op behandeling eenvormig by al hierdie gevalle was, word daar gemeen dat die middel doeltreffend is ten gevolge van sy farmakologiese effek. Dit is onwaarskynlik dat die verkreë verligting psigologies was. Pasiënte wat met fenobarbitoon alleen behandel is, het nie dieselfde vinnige reaksie getoon nie, en daarom is die gevolgtrekking gebillik dat die fenobarbitoon op sigself waarskynlik nie verantwoordelik vir die verligting van die simptome was nie.

Dit skyn asof Tral 'n geskikte terapeutiese middel vir die behandeling van peptiese swere en 'n geprikkelde kolon is. Dit is veral doeltreffend omdat dit minimale newe-effekte het. In vergelyking met ander anticholinergiese middels skyn dit asof Tral 'n breër reaksie het, veral by pasiënte wat aan 'n geprikkelde kolon ly.

CRANIOSTENOSIS, ASYMMETRY AND GROWTH OF THE SKULL

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There is a group of cases with asymmetry of the skull, due to unilateral intracranial or cranial pathology, that is particularly interesting for the study of skull growth because the apparently unaffected side acts as a natural control. It is worth reviewing these and applying the knowledge gained to the differential diagnosis of the craniostenoses.

RADIOLOGICAL ANATOMY

The sphenoidal fissure view is of particular value in the study of asymmetry of the skull as well as in the study of intracranial pathology. Its anatomy will therefore be considered in detail. The radiographs should be examined, as in any other medical examination, in an

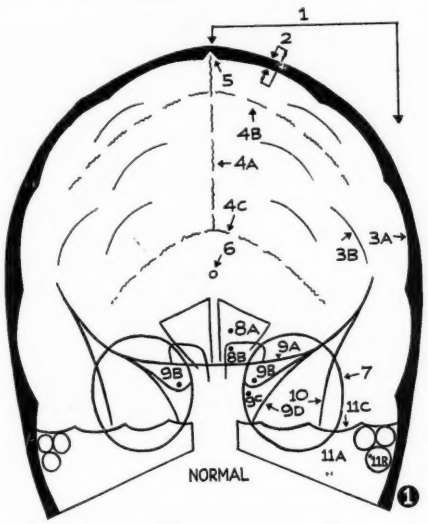
orderly fashion. The following anatomical features are to be observed in this view (Fig. 1, to which the numerals refer):

A. In the Vault.

1. The size and general shape of the hemicrania.
2. The thickness of the vault.
3. The convolutional impressions or digital marks on the inner table, in profile (3*a*) and *en face* (3*b*).
4. The sutures: sagittal (4*a*), coronal (4*b*) and lambdoid (4*c*).
5. The groove for the superior sagittal sinus.
6. The pineal, if visible, for displacement.

B. In the Base.

7. The orbits for size and position.
8. The frontal (8*a*) and the ethmoid (8*b*) sinuses.
9. The sphenoidal ridges (9*a*), and the lesser wings of the sphenoid (9*b*) and the sphenoidal fissures (9*c*) bounded laterally by the medial margin of the greater wings (9*d*). This complex will be referred to as the 'lesser wing' hereafter.
10. The lateral margins of the greater wings of the sphenoid, or the linea innominata.[4]
11. The petrous temporal bone, for its position (11*a*) and pneumatization (11*b*), and for the convolutional impressions on its upper surface (11*c*).



The Towne-Twining view may sometimes be better to show the relative size of the hemicrania; and the basal and lateral views are also necessary. The relevant points of their anatomy will be considered with the first case.

CLASSIFICATION OF CRANIAL ASYMMETRY

Asymmetry of the skull may be classified as due to:

1. *Intracranial Causes.*

(*a*) *Excessive growth stresses*:

i. Extra-cerebral, e.g. chronic subdural haematoma, aneurysm of the internal carotid artery.

ii. Intra-cerebral, e.g. slow-growing tumours, infiltrating lesions and cysts.

(*b*) *Deficient growth stresses*: e.g. the cerebral atrophies, including Sturge-Weber syndrome.

2. *Cranial Causes.*

(*a*) Deficient growth at the sutures, i.e. craniostenosis.

(*b*) Excessive growth, ? analogous to hemivertebrae.

3. *Extracranial Causes.* These may be endogenous or exogenous stresses, or a combination of the two, e.g. with prolonged recumbency, torticollis, etc.

INTRACRANIAL PATHOLOGY: EXCESSIVE GROWTH STRESSES

A CASE OF CHRONIC SUBDURAL HAEMATOMA IN A CHILD

A girl aged 8 years was admitted for a transient attack of weakness of the right hand, inability to speak and headache lasting about 45 minutes. From early infancy she had been unable to look up with her right eye and the left side of the head bulged.*

There was a diffuse bulge in the left temporoparietal region. Looking up caused the right eye to turn outwards and upwards. In the right arm there was slight falling away and purposive movement was often clumsy. All other clinical findings were normal.

The cerebrospinal fluid pressure was 110 mm. of water. The fluid was clear, with no cells and a total protein of 50 mg. per 100 ml. The Wassermann reaction was negative. The electroencephalogram showed a mild generalized slow dysrhythmia, with a silent area in the left parieto-occipital region.

The sphenoidal fissure view (Fig. 2) shows the following abnormalities in the left side:

The hemicranium is enlarged with a thin vault and a smooth inner table (2 in Fig. 2). The lambdoid suture is widened (4*c* in Fig. 2) The lesser wing of the sphenoid is elevated (9 in Fig. 2) and the linea innominata is displaced laterally.

The sagittal suture is vertical (4a). Pneumatization is symmetrical but retarded. The orbits are horizontal, and the superior surfaces of the petrous bones are equally indented.

The basal view (Fig. 3) show the normal anatomical landmarks on the right, and their displacement on the left. The letters indicating the abnormal landmarks are marked with a dash. The landmarks are:

A. The anterior wall of the anterior fossa formed by the squamous portion of the frontal bone.

B. The anterior wall of the middle fossa, a curved line formed by the greater wing of the sphenoid.

*Throughout this paper the lesions, for convenience, are referred to the left side of the skull.

C. The lateral wall of the middle fossa.

D. The posterior wall of the middle fossa, formed by the petrous temporal bone.

E. The posterior wall of the posterior fossa.

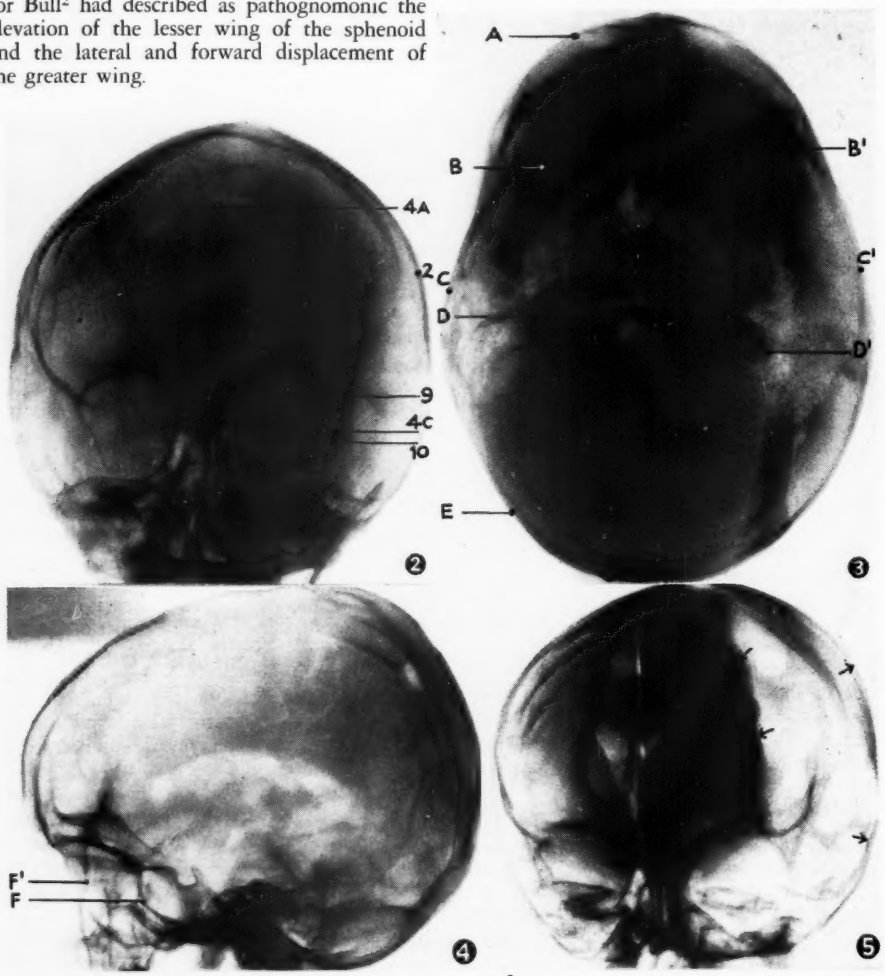
On the pathological side the middle fossa buges forwards and laterally and a little posteriorly.

In the lateral view (Fig. 4) the significant feature is the floor of the middle fossa. On the right it is normal (F), and on the left it is considerably displaced forwards and downwards (F'). This finding is unreliable, as slight deviation from the true lateral position will imitate displacement.

At this stage a diagnosis of chronic subdural haematoma or hygroma seemed straightforward, for Bull[2] had described as pathognomonic the elevation of the lesser wing of the sphenoid and the lateral and forward displacement of the greater wing.

Ventriculography burr-holes (Mr. E. Kerr) showed that the dura on the left side was bluish and atrophic. A large quantity of clear fluid was replaced by air. The right cerebral cortex was normal, though closely pressed up against the dura. The right lateral ventricle was situated more laterally than normal at a depth of 5 cm. Air replacement was performed.

Radiography now (Fig. 5) shows a large quantity of air over the left cerebral hemisphere (arrows). The ventricles are displaced to the right with dilatation of the right lateral ventricle and with depression of the roof of the left lateral ventricle. The third ventricle is tilted to form an angle with the vertical septum



pellucidum. Bull[2] described these features as typical of a subdural haematoma.

At operation Mr. R. A. Krynauw found a large, subdural cyst, containing clear fluid and lined by a firm membrance 2 mm. thick. It covered the superior surface of the left cerebrum and extended on to the inferior and medial surfaces. It was stripped from the arachnoid and from the inner table and the endosteal layer of the dura was removed. Recovery was uneventful.

Prof. B. J. P. Becker reported that the membrane consisted of hyaline connective tissue lined in part by arachnoidal cells and showing a few typical Pacchionian corpuscles and cells containing haemosiderin. It was consistent with the capsule of a chronic subdural haematoma.

Hardman[8] described thinning and bulging of the vault in relation to chronic subdural haematoma, and he noted that Bright[1] had observed this phenomenon.

Davidoff and Dyke[5] described the following signs of juvenile relapsing subdural haematoma:

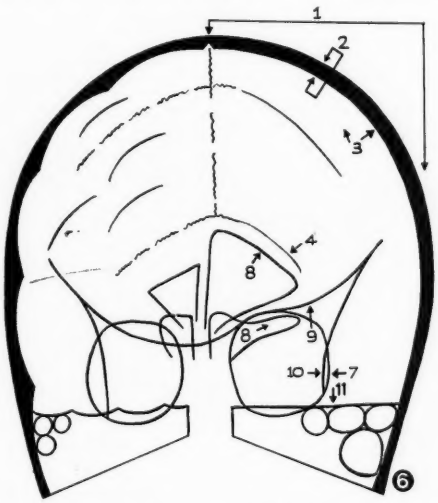
1. Elevation of the sphenoid ridge, the superior orbital plate and the superior orbital ridge (9 in Figs. 2, 6 and 7).
2. Deepening, widening and lengthening of the middle fossa (B′C′D′ in Fig. 3, and F′ in Fig. 4).
3. Disappearance or indistinctness of the oblique line in the orbit (linea innominata) (10 in Figs. 6 and 7).
4. Atrophy of the superior and lateral walls of the superior orbital fissure (Fig. 2).
5. Hypertrophy of the frontal and ethmoid sinuses (8 in Fig. 6).

Bull confirmed the first three of these signs which he summarized as:

1. Elevation of the lesser wing of the sphenoid.
2. Lateral bulging of the greater wing.
3. Forward bulging of the middle fossa.

He considered that these signs were to be expected in a growing malleable skull, where there was an expanding lesion in the middle fossa. Davidoff and Dyke, whose cases had thickened hemicrania, predicted the occurrence of a thin vault on the enlarged side during the growth of the haematoma. The thinning is associated with a loss of convolutional impressions because the inner table is protected from the direct influence of the growing brain by the interposition of the haematoma. This is what occurred in this case, and it is represented diagramatically in Fig. 7.

It is commonly overlooked in the natural history of chronic subdural haematoma that the haematoma may shrink, or shrink and grow



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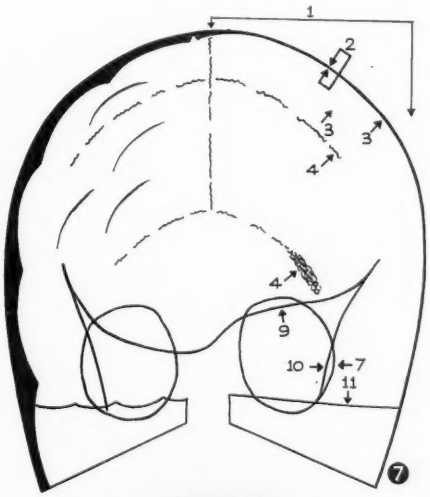

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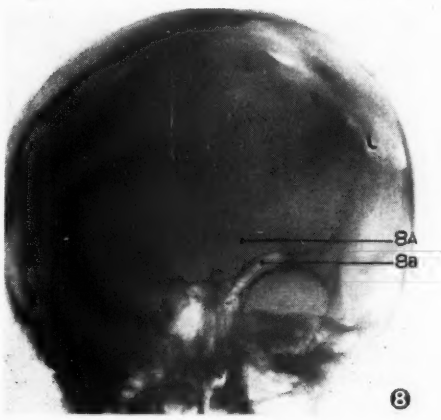

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alternately and also that at any time and at any stage it may be responsible for symptoms by local acute changes in the cerebral haemodynamics that will not be reflected in the radiographs.

The subsequent thickening of the vault is usually due to cerebral atrophy rather than to absorption of the haematoma, though it may be due to either or to both. Davidoff and Dyke thought that there was no radiological evidence of convolutional atrophy in their cases, but in two the inner table was thick and smooth indicating intracranial shrinkage which could have been due to such atrophy. Cerebral atrophy is common with a chronic subdural haematoma as the sequel of either the original injury itself or the pressure of the haematoma. In three of Bull's cases the skull was smaller and there was cerebral atrophy on the affected side. This means that the extent of the atrophy of the brain was greater than the extent of the growth of the subdural haematoma.

This patient was examined 3 years and again 6 years (Fig. 8) after the operation. Clinically she was well. The size and shape of the vault were unchanged. The left side remained thin and smooth, but the right had become thick and had lost its convolutional impressions. The wings of the sphenoid were unchanged. The frontal sinuses and the left ethmoid air cells had developed remarkably rapidly, and the ethmoid cells extended deep into the orbital plate of the frontal bone (8*a* and 8*b* in Fig. 8). On the 3-year study the sinus development was almost confined to the frontals but little further development occurred here in the next 3 years while the ethmoid cells developed.

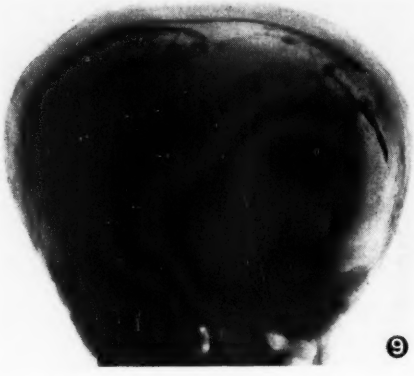
This is an interesting change in emphasis from the frontal to the ethmoid air cells. It probably occurs because of the limits imposed by the normal growth potential of these sinuses. The hypertrophy of the sinuses is predominantly unilateral, indicating a local response to a local lack of growth pressure and not to a low hydrostatic pressure which would have produced a bilaterally symmetrical response.

The absence of thickening of the vault where the haematoma had been removed and its presence on the normal side was unexpected. On the normal side the thickening is a cranial response to the removal of the pressure exerted by the growing brain as it was pressed against the inner table by the haematoma on the opposite side. Why did this thickening not occur on the side where the haematoma had been removed? The inner table is formed by the endosteum, which here had been stripped. This provides a nice demonstration of the function of the endosteum. The persistence of a widened suture on the left side suggests that an intact endosteum may be necessary for sutural ossification.

The next case shows the extent to which changes may occur in the skull in untreated chronic subdural haematoma.

A CASE OF BILATERAL CHRONIC SUBDURAL HAEMATOMA

This was a mentally deficient epileptic adult. The enlarged thickened vault (Fig. 9) has a smooth inner table with no convolutional impressions. The sinuses are tremendously hypertrophied. There are bilateral calcified subdural haematomata.[14] In the lateral view (not reproduced) according to McGregor's criteria,[15] there is platybasia which, in this case, is secondary to the cranial enlargement and not a cause thereof.



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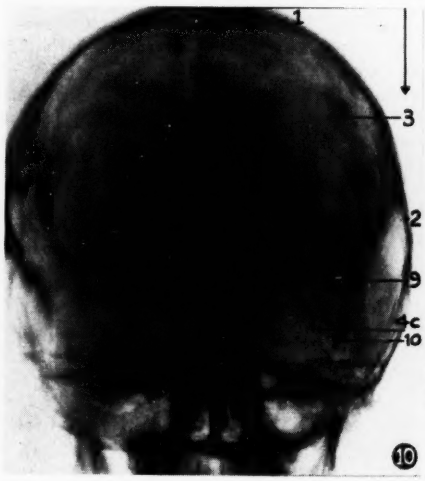
The skull is large because at some stage excessive growth has occurred. During this stage the vault would have been thin so as to resemble a hydrocephalic for which it must not be mistaken.[10] Later, with absorption of the haematoma and atrophy of the cerebrum, the inner table has responded by thickening, and the paranasal sinuses by hypertrophy. These changes are essentially a response to intracranial growth and not to hydrostatic pressure, but at any stage a patient like this, with all the radiological signs of intracranial shrinkage, may develop a raised intracranial pressure due to acute oedema or haemorrhage.

A CASE OF CYSTIC ASTROCYTOMA OF THE TEMPORAL LOBE

A boy of 8½ years was admitted for frequent left frontal headaches following a blow on the head 2 years before. Radiography for fracture

was then reported as negative. Clinical examination was normal except for fullness in the left temporal region. The present radiographs (Figs. 10–12) show an enlarged thin left hemicranium with exaggerated convolutional impressions (1, 2 and 3 in Figs. 10 and 12). The sagittal suture is vertical (*4a* in Figs. 10 and 12) and the left lambdoid suture is widened (*4c* in Figs. 10 and 12). The left orbit is larger and slightly lower, the left lesser wing of the sphenoid is elevated and the linea innominata bulges laterally (9 and 10 in Figs. 10 and 12). The left petrous temporal is depressed and the left temporal squame is thin and bulging. Pneumatization is symmetrical. The basal view shows enlargement of the left middle fossa (B′ C′ D′ in Fig. 11). The findings on the sphenoidal fissure view are illustrated diagramatically in Fig. 12. Radiographs taken 2 years before (Fig 13) showed the same abnormalities with in addition, widening of all the sutures and a generalized exaggeration of the convolutional impressions amounting to a silver-beaten appearance.

At operation Mr. D. Gamsu removed a large cystic astrocytoma occupying the whole of the



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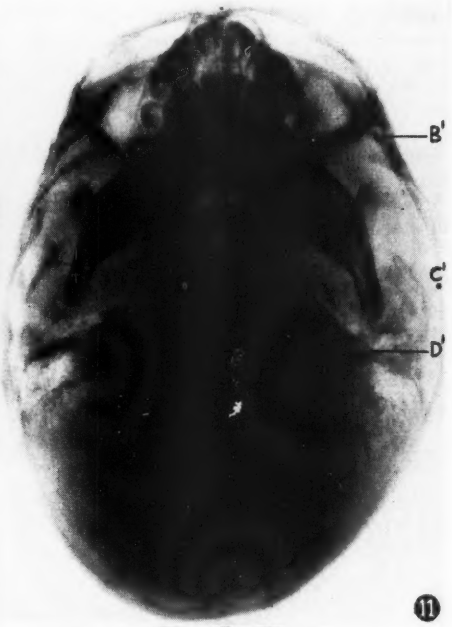

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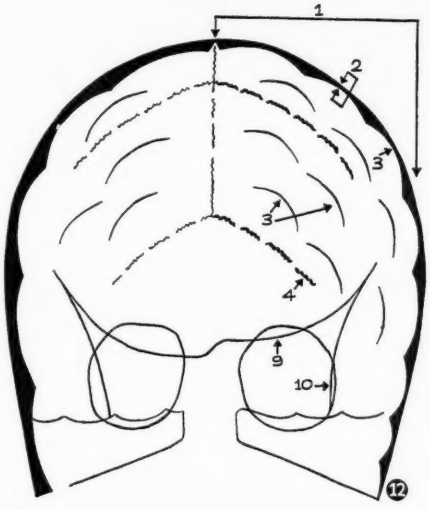

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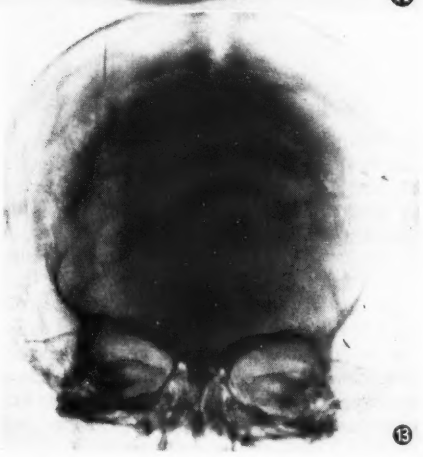
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left temporal lobe. This cyst contained a typical tumour nodule.

The elevation of the lesser wing of the sphenoid and the bulging of the greater wing suggested a chronic subdural haematoma, as these signs had been called pathognomonic. The marked convolutional impressions did not conform to the interposition of a chronic haematoma between the convolutions and the inner table, and Bull[2] had already predicted these changes with a temporal lobe tumour.

The wide sutures and the marked convolutional impressions were thought to be normal at the first examination, but the abnormalities in the middle fossa had been overlooked. The reversion of most of the sutures to normal width in the 2 years contrasts with the persistent widening of the left lambdoid suture in Case 1. It did not mean that the tumour had stopped growing, but merely that the rate of growh had decreased so that ossification could catch up with it.

In addition to the local changes in the middle fossa the original examination showed widening of the sutures and a diffuse silver-beaten appearance. Either the cerebrum increased in volume (due to hydrocephalus or possibly to some other change such as excessive vascularity) or the growth of the tumour caused the whole brain to be uniformly pressed up against the inner table.

A CASE OF LEUCO-ENCEPHALITIS

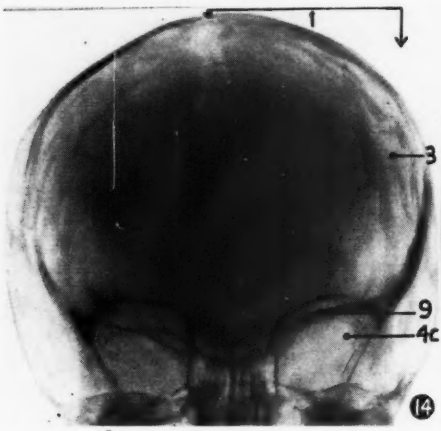
A girl aged 6 years was admitted for concussion following a fall. She was X-rayed to exclude a fracture and asymmetry of the skull was observed. On the left the hemicranium was larger, the convolutional markings were exaggerated, the lesser wing was elevated, and the lambdoid suture was widened (1, 3, 9 and 4*c* in Fig. 14). The basal view was normal.

A slowly growing intracranial mass was suspected but the patient was discharged. One month later she was re-admitted for insomnia, restlessness, fatigue and excessive yawning. There was now a history of brief attacks of unconsciousness from the age of 4 months, occurring 3 times a year, lasting a few moments, and sometimes accompanied by a fall, and also of frequent headaches but not of convulsions.

The clinical examination and the cerebro-spinal fluid were normal. The air encephalogram (Fig. 15) showed bizarre displacement of the lateral ventricles, with widening of the septum pellucidum.

Burr holes revealed no subdural haematoma. A needle biopsy showed 'a diffuse chronic infiltrating lesion of the white matter having the characteristics of a leuco-encephalitis'.

Intracranial pathology of long duration was suspected on the first examination because of the asymmetry which did not conform to the patterns due to cranial or extracranial causes. The pattern was that of a large slowly growing mass. In spite of the absence of enlargement of the middle fossa, a temporal lobe tumour was considered but it was not confirmed by the air studies; nor could it account for the widened septum pellucidum. The histological diagnosis of a diffusely infiltrating lesion of the white matter, related to an infiltrating gliosis, accounted for the cranial evidence of asymmetrical cerebral enlargement as well as for the thickening of the septum pellucidum and the unusual displacement of the lateral ventricles.



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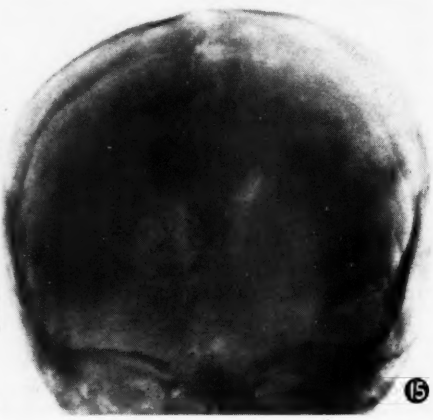
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(To be continued)

SKELETAL CHANGES IN ENDOCRINE AND METABOLIC DISORDERS

XVII. RICKETS DUE TO VITAMIN D DEFICIENCY

W. P. U. JACKSON, M.D., M.R.C.P., D.C.H.
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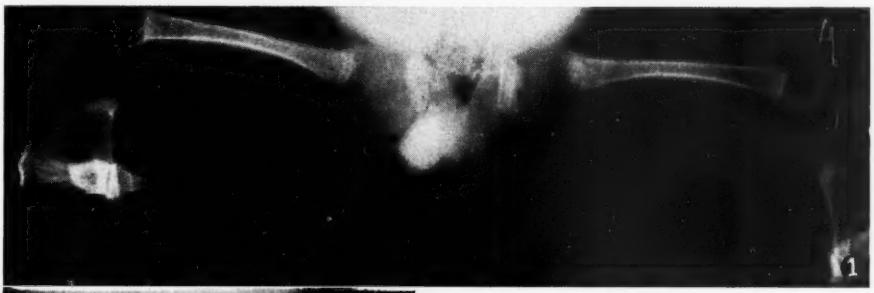
The proximate cause of rickets is an insufficiency of calcium phosphate with which to impregnate a normally deposited organic bone matrix. The serum inorganic phosphate is low, but the serum calcium is usually normal (probably kept up by parathyroid activity). The alkaline phosphatase is raised, suggesting an excessive osteoblastic activity. Calcium virtually disappears from the urine. In the rickets of malnutrition a lack of vitamin D is the etiological factor, since this vitamin is responsible for ensuring good absorption of calcium and phosphorus.

The clinical features will not be discussed here.



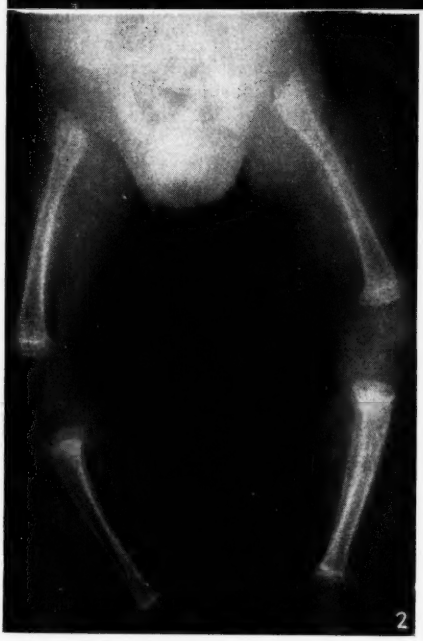
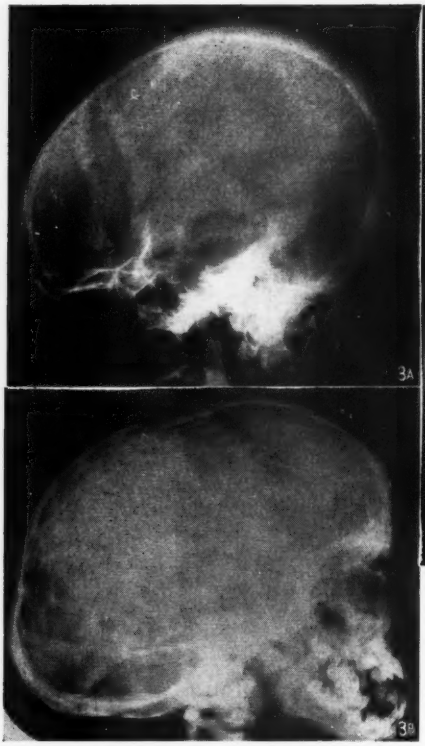


Fig. 1. Florid rickets in a premature infant. Note the fluffy cup-shaped expansion at the bone ends and the great distance of the tibia from the femur. *Fig. 2.* The same case, healing. Note the new periosteal calcification and filling in of the expanded bone ends. (Case of Prof. F. Ford).

RADIOLOGICAL FEATURES (FIGS. 1–4)

1. *Active Rickets.* As already remarked, the basic lesion is a non-calcification of osteoid tissue (bone matrix). On an X-ray of a growing bone end the clear uncalcified area between the epiphysis and the diaphysis is excessive. The metaphysis is irregular and its margin fluffy. It becomes widened or splayed out, corresponding with the obvious clinical enlargement of the wrists and costo-chondral junctions. In the child under 6 months the skull may be outstandingly involved, with thinning of the occipital and parietal regions and later thickening of the outer table in the region of the frontal and parietal eminences.

In addition, the whole skeleton becomes poorly calcified and less dense, with generally thin cortices. Secondary bending of bones



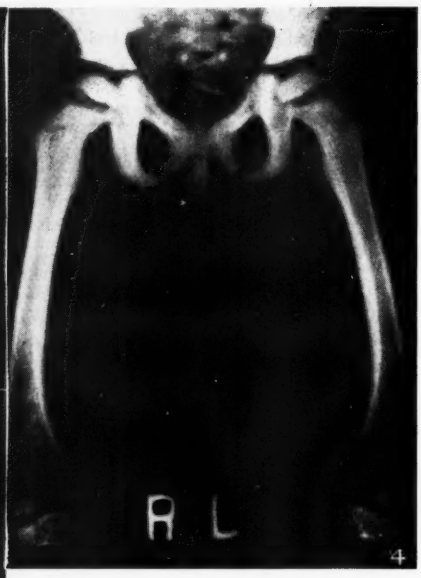


Fig. 3. Skulls from cases of old, healed rickets. Note areas of thinning and thickening in the vault.
Fig. 4. Femora from the case shown in Fig. 3B. Note the coarse trabecular pattern, symmetrical bowing, thickened medial aspects of femoral cortices ('buttressing'), and thick femoral necks. The patient was aged 15 years and was brought to hospital because of dwarfing.

occurs and produces coxa vara, a funnel-shaped or tri-radiate pelvis, curvature of the long bones, with buttressing by added bone in the concave arc, uniform biconcavity of the vertebral bodies, and various deformities of the thoracic cage, e.g. pigeon chest and Harrison's sulcus. The changes are bilateral and symmetrical. True fractures (often greenstick) may occur, but the Looser's zones of adult osteomalacia are not seen.

Growth in length is checked, with eventual stunting, and the appearance of epiphyseal centres is delayed.

2. *Healing Rickets.* The previously radiographically clear zone begins to be filled in, while the 'fuzzy' bone end straightens out and a transverse line of calcification appears at the very end of the shaft, near the epiphysis.

The uncalcified osteoid tissue (which was laid down subperiosteally) begins to calcify, giving the appearance of a 'raised periosteum' which, it is important to realize, does not necessarily indicate scurvy.

3. *Old Healed Rickets.* The subject may be stunted, with some of the aforementioned deformities. In particular, the vault of the skull may show areas of increased thickness, while the bowed long bones retain their concave buttresses. The trabecular pattern, especially well seen in the pelvis, may be abnormally coarse.

4. *Foetal rickets,* evident at birth, is very uncommon, and most cases are reported from China in mothers who themselves have osteomalacia due to vitamin D lack. However, I believe that the occasional case does occur in this country.

OPSOMMING

Rhachitis word kortliks uit die biochemiese oogpunt bespreek.

Die radiologiese kenmerke word vervolgens beskryf, en besonder klem word op die minder bekende verskynsels gelê.

REFERENCES

1. Parsons, L. G. (1934): *Diseases of Childhood.* 3rd ed. (by Garrod, Batten and Thursfield). London: Edward Arnold & Co.
2. Fairbank, T. (1951): *Atlas of General Affections of the Skeleton.* London: E. & S. Livingstone Ltd.

RECOVERY AFTER AN INTRAVASCULAR HAEMOLYTIC BLOOD TRANSFUSION

REACTION CAUSED BY ANTI-KELL IN THE RECIPIENT'S BLOOD

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and

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The object of this article is to emphasize the importance of using the indirect antiglobulin test routinely in the cross-matching of blood for transfusion. This is illustrated in the case of Mrs. G., who suffered a severe haemolytic reaction as a result of the presence of Kell antibody in her blood stream.

Mrs. G.'s blood was sent to the Johannesburg Centre for ante-natal investigation in February 1951. Her history is shown in Table 1.

TABLE 1: MRS. G'S ANTE-NATAL HISTORY

Previous Pregnancies	*Date of Termination*	*Gestation Period*	*Nature of Termination*	*Outcome*
1st	28 May 1944	8 months	Normal delivery	Normal
2nd	8 June 1946	9 months	Caesarean section (*placenta praevia)	Died
3rd	3 August 1948	6 months	Premature delivery	Died
4th	20 May 1950	9 months	Normal delivery	Died (Liver enlarged)

*Blood transfusion 1946 for haemorrhage due to placenta praevia.

In February 1951 she was not pregnant and her doctor wished to investigate the cause of the neo-natal deaths.

Her serological tests showed that she was group A, Rh negative, that incomplete Rh_0 antibodies were present in a titre of 1:256 and blocking antibodies to a level of 1:16.

Her husband was group O, Rh_1Rh_2 (probable genotype, R_1R_2).

In April 1952 her blood was re-investigated since she was pregnant again. The antibody titres were: Nil in saline; 1:256 in serum albumin; 1:256 with papainated cells and 1:8 blocking antibodies. The titres remained at this level except for the one in serum albumin, which rose to 1:1024 on 1 September 1952 when the pregnancy terminated in a still-birth.

Shortly afterwards she was asked to give a donation of her blood for the preparation of anti-Rh_0 testing serom; but in view of a slight anaemia it was decided to give her a transfusion to replace the donated blood. As she lived about 40 miles from Johannesburg and found it impossible to visit the Transfusion Centre to be bled, a centrifuge was taken to her home so that compatibility tests could be done on the spot. On 29 October 1952, a pint of her blood was withdrawn and immediately afterwards a pint of group O, Rh negative blood was administered. A simple rapid cross-matching test performed between Mrs. G's serum and a saline suspension of the donor's cells showed no incompatibility.

Apart from transient flushing of the face, Mrs. G. showed no evidence of reaction during the transfusion. About half an hour after the end of the transfusion, however, she experienced a severe rigor, vomited and became collapsed. The next day she passed dark, port-wine coloured urine which showed the spectroscopic absorption bands of methaemoglobin. Schumm's test on her blood was positive and further investigation revealed that she had anti-Kell in addition to anti-Rh_0 in her serum. Re-examination of the donor blood showed it to be group O, Rh negative, Kell positive.

The patient's fluid intake was restricted to 1 litre a day from the second day after the transfusion. Intermittent vomiting continued

until the twelfth day, but its amount was recorded only from the seventh day. Table 2 records the input-output chart from the seventh day.

The urinary output dropped to 45 c.c. on each of the eighth and ninth post-transfusion days, improving progressively on the tenth, eleventh and twelfth days, with pronounced polyuria from the thirteenth day.

Slight jaundice appeared on the second post-transfusion day and disappeared within a week.

Apart from the initial collapse (from which she recovered quickly), her general condition remained good until she showed signs of drowsiness on the seventh day, with a slight rise in blood pressure.

During the 24 hours of the eighth day she was given an intravenous infusion of 1,500 c.c of a solution containing the following ingredients:

Dextrose	100 g.
Ethyl Alcohol 98%	50 g.
Sodium Chloride...	6.0 g.
Sodium Lactate	4.5 g.
Aq. Dest. ... ... *ad*	1,500 c.c.

During this period of 24 hours only 45 c.c. of urine were passed and 385 c.c. of vomitus brought up (Table 2).

Although there was no immediate increase in urinary output, her general condition improved immediately. Her serum potassium, however, remained at the unsatisfactory level of 7.2 mEq./L (Table 3).

In view of the alarming state of her blood electrolytes on the sixth day (Table 3), preparations had been made for a replacement

TABLE 2: FLUID INTAKE AND OUTPUT IN C.C. FROM THE SEVENTH TO THE FOURTEENTH DAY

Day	*Date November* 1952	*Volume (c.c.) Intake*	*Route*	*Volume (c.c.) Output* *Vomitus*	*Volume (c.c.) Output* *Urine*
7	5	1000	Oral	300	225
8	6	1360 1000	Intravenous Oral	385	45
9	7	500	Blood	360	45
10	8	1000	Oral	180	330
11	9	1000	Oral	480	480
12	10	1000	Oral	60	990
13	11	2000	Oral	0	Polyuria (amounts not recorded)
14	12	Full diet			

TABLE 3: BLOOD CHEMISTRY BEFORE AND AFTER INTRAVENOUS THERAPY

	Before Intravenous Therapy (Sixth Day)	*After Intravenous Therapy (Ninth Day)*	*Polyuria Thirteenth Day)*	*Normal Range*
Blood Urea	460 mg. per 100 ml.	288 mg. per 100 ml.	304 mg. per 100 ml.	15–40 mg. per 100 ml.
CO_2 Combining Power ..	8·1 mEq/L	13·0 mEq/L	14–0 mEq/L	24–35 mEq/L
Chlorides (as NaCl) ..	86 mEq/L	92 mEq/L	98 mEq/L	95–106 mEq/L
Sodium	119 mEq/L	137 mEq/L	132 mEq/L	136–150 mEq/L
Potassium	7·1 mEq/L	7·1 mEq/L	6·3 mEq/L	3·9–5·6 mEq/L

transfusion. However, in view of the improvement in her condition, this became unnecessary.

A haemoglobin estimation on the ninth day showed the level to be 9.7 g. % and she was therefore given 500 c.c. of group A Rh negative, Kell negative blood, without untoward reaction.

With the commencement of polyuria on the thirteenth day, she was allowed 2,000 c.c. of fluid by mouth per day. On the fourteenth day she ceased vomiting for the first time and was placed on a full diet. Her blood electrolyte pattern, when diuresis commenced, is shown in Table 3.

Her blood urea was still high on 10 January 1953, i.e. 2 months after the haemolytic transfusion reaction.

Kidney function tests performed on 23 April 1954 showed slightly abnormal kidney function (Table 4).

TABLE 4: KIDNEY FUNCTION TESTS (23 APRIL 1954)

Test	*Result*
Blood Urea	31 mg. per 100 ml.
Urea Clearance..	108%
Maximum Urine Concentration	1016 Sp. Gr.
Microscopic and Chemical ..	Normal
Blood Pressure	120/77 mm. Hg.

The Fishberg concentration test showed that Mrs. G. was unable to concentrate to the normal specific gravity limit of 1022 and therefore had not regained completely normal renal functions 18 months after the accident.

SEROLOGY

After the patient's intravascular haemolytic reaction, the bloods of the donor and patient were carefully matched at three temperatures (Table 5).

It will be seen that no incompatibility was detectable in the major compatibility test (i.e. patient's serum against donor's cells suspended in saline and in AB serum) after prolonged incubation at the 3 temperatures specified. Only after the indirect antiglobulin test had been applied was the incompatibility evident.

On testing the patient's cells with type specific sera, her phenotype was found to be Group A, Rh negative (cde/cde), MMss, P+, Fy^a+, kk, Lu−.

The donor was group O, Rh negative (cde/cde), MMss, P+, Fy^a+, Kk, Lu−.

The husband was group O, R_1R_2 (CDe/cDE), MNss, P−, Fy^a+, Lu−, kk.

DISCUSSION

As the husband was Kell negative, it is reasonably certain that she was sensitized to the Kell antigen not by her pregnancies, but as a consequence of the transfusion in 1946. Since anti-Kell was present in her serum a day after the transfusion in 1952, it can also reasonably be assumed that the Kell antibody was present at the time of the second transfusion.

Race and Sanger[1] state that many examples of the Kell antibody have been recognized, usually as a result of haemolytic disease of the newborn, or transfusion reactions.

Otensooser *et al.*[2] reported on a case with fatal outcome due to anti-Kell. This case is very similar to that of Mrs. G., in that it demonstrated the dangerous nature of the Kell antibody. It also showed, as in Mrs. G.'s case, that a single transfusion of Kell positive blood to a Kell negative recipient can apparently produce antibodies which persist for many years and that such antibodies are capable of producing immediate and severe reactions with subsequent transfusions of Kell positive blood.

The antiglobulin test has been used routinely in this Service as part of the incubated cross-match test since 1950, being departed from only in extreme emergency, or in those rural divisions of the Service where no full-time technicians are available. The antiglobulin test will detect most of those incompatibilities due to incomplete antibodies which will not be detected in the ordinary cross-matching test between a saline suspension of donor cells and

TABLE 5: SEROLOGICAL REACTIONS OF THE PATIENT'S SERUM WITH DONOR'S CELLS AT THREE TEMPERATURES
Patient's Serum versus Donor's Cells

	4°C. (2 hours)	*Room Temperature* °C. (2 hours)	37°C. (2 hours)
Donor's cells in saline ..	Negative	Negative	Negative
Donor's cells in group AB serum ..	Negative	Negative	Negative
Titre of indirect Antiglobulin test (anti-Kell)	1:64	1:128	1:128

the serum of the patient. The test was omitted in the case described owing to the difficulty of obtaining a pre-transfusion specimen for testing in the laboratory and the accident would certainly have been avoided if this precaution had been taken.

SUMMARY

1. A severe haemolytic reaction caused by anti-Kell, formed in a patient's serum by a previous blood transfusion, and its successful treatment by fluid restriction, correction of electrolyte imbalance and administration of compatible blood, is described.

2. The necessity for performing the indirect antiglobulin test, as part of the routine cross-matching test, is emphasized.

3. Kidney function remained slightly abnormal even 18 months after the incompatible transfusion reaction.

OPSOMMING

1. 'n Ernstige hemolitiese reaksie, veroorsaak deur anti-Kell, is in 'n pasiënt se serum gevorm deur 'n vorige bloedoortapping, en die suksesvolle behandeling daarvan deur vloeistofbeperking, die verbetering van elektrolitiese onewewigtigheid, en die toediening van verenigbare bloed word beskryf.

2. Die noodsaaklikheid vir die uitvoering van die onregstreekse antiglobulientoets as deel van die roetine-kruisaanpassingstoets word benadruk.

3. Die nierfunksie was effens abnormaal selfs 18 maande ná die onverenigbare bloedoortappingsreaksie.

The assistance of Dr. B. M. Bloomberg with the blood chemistry and the kidney function tests is gratefully acknowledged. These tests were performed in the laboratories of Drs. S. Sims, J. Gluckman, B. M. Bloomberg and W. Lewin, Pathologists, Johannesburg.

The advice of Prof. H. B. Stein, with regard to the preparation of the intravenous solutions and his assistance with biochemical tests, is much appreciated. This work was performed in the Department of Clinical Pathology, University of the Witwatersrand, Johannesburg.

We wish to thank Drs. H. Feldman and W. Sacks for their help.

The technical assistance of Senior Technician A. Irvine is appreciated.

REFERENCES

1. Race, R. R. and Sanger, R. (1954): *Blood Groups in Man,* 2nd ed., p. 223. Oxford: Blackwell Scientific Publications.
2. Otensooser, F., Mellone, O. and Biancalana, A. (1953): Blood, **8,** 1029.

NOTES AND NEWS : BERIGTE

Mr. C. A. R. Schulenburg, of Pretoria, has left for Europe, accompanied by his wife.

Mr. Schulenburg will be visiting surgical clinics in England and on the Continent.

* * *

Mr. Jack Penn, F.R.C.S., of Johannesburg, leaves on 28 March for a short visit overseas. On his way he will stop at Lamberene where he will work on elephantiasis at Dr. Albert Schweizer's clinic. His next stop will be in Italy where he has been invited to lecture at the University of Milan. He will then proceed to Israel where he will inspect and lecture in the Department of Plastic Surgery at the University of Jerusalem in his capacity of Visiting Professor of Plastic Surgery. Mr. Penn expects to return to Johannesburg at the end of April.

* * *

NAPT COMMONWEALTH CHEST CONFERENCE

OPENING 1 JULY 1958

Commonwealth problems will be given special emphasis, but as chest diseases are a matter of international concern, the speakers will include some of the foremost authorities from many parts of the world and visitors from all countries will be welcome. Although the campaign against tuberculosis is well on the way to success in many countries such as Scandinavia, Great Britain and the United States, the disease is still a serious menace in others, especially in the tropics.

The first subject on the programme is The World Anti-Tuberculosis Campaign—Is It Succeeding? and speakers include Dr. Johannes Holm (*World Health Organization*), Sir Harry Wunderly (*Australia*), Dr. B. A. Dormer (*South Africa*), Sir Kenneth Cowan (*Scotland*), Dr. J. H. F. Jayasuriya (*Ceylon*), Prof. R. Neubauer (*Yugoslavia*).

Among other subjects are: *The Heart Patient in Everyday Life*; *The Family and the Patient with Chest Disease—How Best Can We Help Them to Help Themselves?*; *The Patient's Personality*; *The Problem of Lung Cancer; Tuberculosis and Leprosy* —Dr. F. A. H. Simmonds, Dr. Grove-White (*Singapore*) and other speakers—and Tuberculosis Medical and Social Services in the British Commonwealth—speakers include Dr. W. S. Haynes (*Kenya*), Dr. R. Lavoipierre (*Mauritius*), Dr. A. A. Cameron (*Federation of Malaya*) and Dr. H. N. Davies (*Tanganyika*).

An extensive Exhibition to be held in the foyers of the Royal Festival Hall during the Conference will illustrate, among other things, the modern drugs and equipment used in the preventive treatment of chest diseases. Manufacturers of pharmaceutical products, X-ray apparatus and photographic materials, surgical instruments and hospital equipment will be staging special exhibits.

Visits to hospitals and clinics and tours of general interest will be arranged during the 3 days immediately following the sessions. Plans have already been completed for visits to the Enham-Alamein Village Centre, Andover; Grove Park Hospital; Harefield Hospital; High Wood Hospital for Children; Great Ormond Street Hospital for Sick Children; Stoke Mandeville Hospital, Aylesbury; Papworth Village Settlement; King Edward VII Sanatorium, Midhurst; and a Mass Radiography Unit.

Full particulars of the Conference can be obtained from the Secretary-General, NAPT, Tavistock House North, Tavistock Square, London, W.C.1.

DEPARTMENT OF SURGERY, UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

INVITATION CLINICAL LECTURES, FINAL YEAR STUDENTS AND ANY POSTGRADUATES

TUESDAYS 12-1, IN THE HOSPITAL LECTURE THEATRE

1958		Lecturer	Title
March	25	Mr. J. Lannon ..	*Peripheral Vascular Diseases.*
April	1	Mr. Trehair ..	*Herniae.*
	8	Mr. Fatti	*Cardiac Surgery.*
	15	Mr. Adler	*Carcinoma of the Lung.*
	22	Mr. Douglas ..	*Evaluation of Jaundice and Bile Duct Surgery.*
	29	Mr. Almond ..	*Gall Bladder Surgery.*
May	6	Mr. Theron ..	*Surgical Management of Liver Cirrhosis.*
	13	Dr. E. Samuel ..	*Radiology of the Acute Aspect of Duodenal Ulcer and Intestinal Obstruction.*
	20	Mr. Cuthbert ..	*Carcinoma of Face and Mouth.*
	27	Mr. Mace-David ..	*Swellings of the Neck.*
June	3	Mr. J. Wolfowitz	*The Breast — Epitheliosis, Fibrosis and Carcinoma.*
	10	Mr. Girdwood ..	*Abdominal Fistulae.*
	17	Mr. Brayshaw ..	*Haematuria.*
	24	Mr. J. Cuthbert ..	*Scope of Reconstructive Surgery.*
July	29	Mr. Skapinker ..	*The Surgery of the Pancreas.*
August	5	Dr. C. J. Goedvolk	*The Injured Workman.*
	12	Mr. Leonsins ..	*The Surgical Response to Trauma and Real Insufficiency.*
	19	Mr. W. J. Thomas	*Shock and Blood Replacement.*
	26	Mr. Ian McGregor	*The Treatment of Burns.*
September	2	Mr. C. C. Freed	*The Surgery of the Hand.*
	9	Mr. R Fleming ..	*Trauma of the Pelvic Girdle.*
	16	Mr. Kleinot, Mr. Lipschitz and Mr. Bloch ..	*Management of Paraplegic Patients.*
	23	Dr. A. Watt ..	*Evaluation and Treatment of Head Injuries.*
	30	Dr. M. Weinbrenn	*The Present Status of Deep Therapy.*
October	7	Mr. Gordon ..	*Primary and Delayed Primary Wound Suture and Problem of Wound Sepsis.*
	14	Mr. J. A. Douglas and Tutorial Staff ..	*The Approach of Students to Clinical Examinations.*

* * *

INTERNATIONAL FEDERATION OF GYNAECOLOGY AND OBSTETRICS

SECOND WORLD CONGRESS

The Second World Congress of the International Federation of Gynaecology and Obstetrics, which will be held in the newly built Queen Elizabeth Hotel in Montreal, Canada, from 22 to 28 June 1958, will have on its programme 8 main lectures given by eminent scientists whose studies and research are related to the field of gynaecology and obstetrics. The guest speakers and the titles of their lectures are as follows:

Prof. Murray L. Barr, Department of Microscopic Anatomy, University of Western Ontario, London, Canada: *Tests of Chromosomal Sex and their Application to Clinical Problems.*

Prof. Hermann Bautzmann, Anatomisches Institut, Hamburg, Germany: *Comparative Studies on the Histology and Function of Animal and Human Amnion.*

Prof. Roberto Caldeyro-Barcia, Chief of the Section of Obstetrical Physiology, Faculty of Medicine, Montevideo, Uruguay: *Contractility of the Human Gravid Uterus and its Application to the Obstetric Clinic.*

Prof. G. W. Harris, Head of the Department of Neuroendocrinology, Maudsley Hospital, London, England: *Relationship of the Central Nervous System to Pituitary and Reproductive Activity.*

Prof. Charles Oberling, Institut de Recherches sur le Cancer Gustave Roussy Villejuif (Seine), France: *The Cytology of the Cancerous Cell.*

Prof. Bradley M. Patten, Chairman, Department of Anatomy, University of Michigan Medical School, Ann Arbor, Michigan: *The Establishing of Fetal-Maternal Vascular Relations.*

Prof. Hans Selye, Director of the Institute on Experimental Medicine and Surgery, University of Montreal, Montreal, Canada: *Stress in Gynaecology.*

A representative of the U.S.S.R. (on a subject of his choice).

All correspondence should be directed to the Montreal Committee, Second World Congress, International Federation of Gynaecology and Obstetrics, 1414 Drummond Street (Suite 220), Montreal 25, Canada.

* * *

THE NEW PHARMACEUTICAL RESEARCH LABORATORIES OF I.C.I. AT ALDERLEY PARK, CHESHIRE, ENGLAND

A few months ago, the late Lord Waverley, a former Chancellor of the Exchequer, officially opened the new Research Laboratories of I.C.I. Pharmaceuticals Division at Alderley Park. The Alderley Laboratories cover 30 acres of the 350-acre site.

Eminent scientists from universities and colleges from all parts of the United Kingdom attended the opening ceremony.

This new ICI research project costs some £1,500,000 and marks a period of almost 15 years of intensive activity in the pharmaco-therapeutic field.

One of the remarkable features of the Animal Breeding Unit (which is essential for the adequate function of the Biological Laboratories) is the development of a breeding system which will overcome the complications of the common infections inevitably found in commercial stocks of laboratory animals. The small laboratory animal is to the biologist what the test-tube is to the chemist. The Alderley programme permits animals to be removed at term by caesarean section (i.e. by 'sterile birth') and then to be raised artificially. The parents of the future breeding stock can thus be obtained free from their natural diseases. The physical arrangements of the Breeding Unit are designed to maintain this freedom for all time.

ICI research in the pharmaceutical field stretches over only some two decades. This period has been marked, however, by outstanding contributions to the treatment of disease. The organization played an important part in pioneering large-scale penicillin production, in the early days, at the request of Professor Florey and his group of eminent associates.

ICI research has also been responsible for a series of outstanding discoveries in the field of intravenous and inhalation anaesthesia, sulphonamides and other antibacterial agents, and antimalarial and antiepileptic drugs, as well as drugs for the treatment of leprosy. It is, at present, also actively engaged on research into virus infections, tuberculosis and the chemotherapy of malignant disease (e.g. leukaemia).

The magnificent accommodation and facilities at Alderley will undoubtedly speed and spur efforts in the field of medical research. The new laboratories symbolize the imaginative vision which has inspired a remarkable programme of fundamental and applied research.

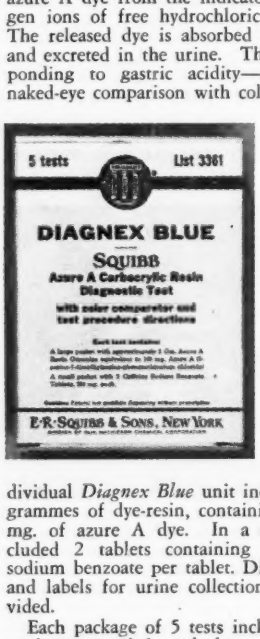
PREPARATIONS AND APPLIANCES

DIAGNEX BLUE FOR TUBELESS GASTRIC ANALYSIS

SQUIBB AZURE A CARBACRYLIC RESIN DIAGNOSTIC TEST

Diagnex Blue makes possible the simple qualitative determination of stomach acidity without the necessity of intubation.

The essentials are supplied in the *Diagnex Blue* package and the method involves a simple change of azure A dye from the indicator resin for the hydrogen ions of free hydrochloric acid in the stomach. The released dye is absorbed into the blood stream and excreted in the urine. The dye content—corresponding to gastric acidity—can be estimated by naked-eye comparison with colour standards.



Wide range of Usefulness: The use of *Diagnex Blue* in the office, clinic or hospital benefits the busy doctor with its time-saving convenience and spares the patient the discomfort of gastric intubation. In addition, as a recent J.A.M.A. Editorial points out, the simplicity and economy of the *Diagnex Blue* test makes it valuable for mass-screening surveys.

Supply: The individual *Diagnex Blue* unit includes a packet with 2 grammes of dye-resin, containing approximately 100 mg. of azure A dye. In a separate wrap are included 2 tablets containing 250 mg. of caffeine sodium benzoate per tablet. Directions to the patient and labels for urine collection bottles are also provided.

Each package of 5 tests includes a comparator for performance of the naked-eye test.

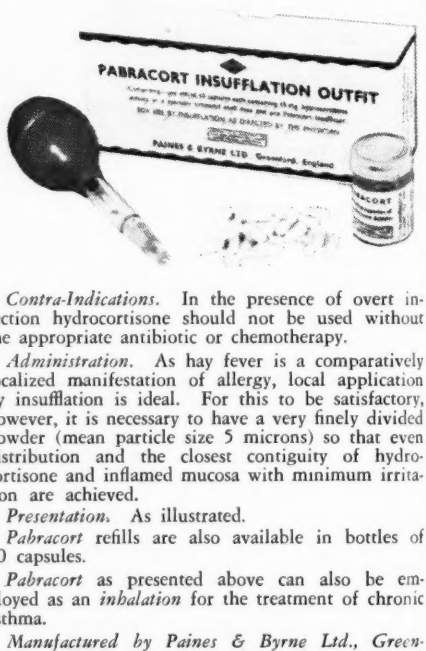
Supplies are available from all wholesale and retail sources.

Manufacturers: Squibb Laboratories (Pty.) Limited, Pharmacy House, 80, Jorissen Street, Braamfontein, Johannesburg.

PABRACORT

Pabracort (hydrocortisone acetate) insufflation outfit is indicated for the treatment of hay-fever (seasonal rhinitis), allergic rhinitis, and uncomplicated allergic asthma. A recent report in *The Lancet*, dated 25 January 1958, pp. 187–188, shows 70% success in chronic asthma patients.

Mode of Action. Hydrocortisone suppresses the cellular and humoral elements of the inflammatory reaction and is especially effective when inflammation is due to allergic factors only. Absorption from the nasal mucosa in allergic rhinitis is sufficient to subdue the coincident conjunctivitis and ameliorate concurrent allergic asthma. Maximum concentration is achieved at the site of the lesion and baneful side reactions, e.g. gastro-intestinal disturbances, are avoided by the topical use of small doses.



Contra-Indications. In the presence of overt infection hydrocortisone should not be used without the appropriate antibiotic or chemotherapy.

Administration. As hay fever is a comparatively localized manifestation of allergy, local application by insufflation is ideal. For this to be satisfactory, however, it is necessary to have a very finely divided powder (mean particle size 5 microns) so that even distribution and the closest contiguity of hydrocortisone and inflamed mucosa with minimum irritation are achieved.

Presentation. As illustrated.

Pabracort refills are also available in bottles of 10 capsules.

Pabracort as presented above can also be employed as an *inhalation* for the treatment of chronic asthma.

Manufactured by Paines & Byrne Ltd., Greenford, England, and Marketed by the Sole South African Distributors: Petersen Limited, P.O. Box 38, Cape Town, and P.O. Box 5785, Johannesburg, from whom further particulars may be obtained.

COMPLAN

A NEW DIETARY AID FOR HOME AND HOSPITAL

Complan is the simple solution to the problem of adequate nourishment when a normal diet cannot be eaten. One pound (450 g.) of *Complan* provides 2,000 calories, balanced amounts of protein, carbo-

hydrate and fat, and all vitamins, minerals and trace requirements. Thus if no ordinary food at all can be eaten, one pound (450 g.) of *Complan* fed by tube or cup each day, can sustain life for indefinite periods. If normal food intake is restricted, smaller amounts of *Complan* provides a valuable dietary supplement.

Complan is administered with ease. It is ready for feeding simply by mixing with water. *Complan's* pleasant taste makes it most acceptable from a cup and, being low in fat and free from starch and wheat gluten, it is remarkably well tolerated, even by weakened digestions.

Complan in the Hospital: It is far easier to prepare a complete, free-flowing tube feed or bland liquid diet with *Complan* than by using normal methods and it takes less time. Other special diets can be more simply prepared with *Complan* because the amount of every nutrient it contains is known precisely.

Complan also solves the problem of a suitable diet for invalids, convalescents and others, unable to eat normal meals, who are nursed at home.

No other food offers such a complete answer to so many feeding problems.

Complan can be given:

(*a*) *As a Tube Feed;* (*b*) *As a Continuous Intragastric Drip;* (*c*) *As a Cup Drink;* (*d*) *In Other Food.*

Indications: (*a*) *As a Sole Diet*: Unconscious patients, e.g. after strokes, head injuries or neurosurgery; patients unable or unwilling to swallow, e.g. in bulbar paralysis due to poliomyelitis, in mental illness; after operations, especially those on the alimentary tract; after plastic or maxillo-facial surgery or burns; gastrostomy cases; ulcer patients, e.g. as an alternative to milk for continuous intragastric drip and as a bland liquid diet.

(*b*) *As a Supplementary Diet*: Invalids, canvalescents, the aged, when food intake is restricted; expectant and nursing mothers, growing children, premature babies, when extra nutrients are needed; special diets requiring high protein-vitamin-mineral intake.

The Complan Formula (per lb.):

Protein	140	g.
Fat	74	g.
Carbohydrate	200	g.
Calcium	3.8	g.
Phosphorus	3.6	g.
Sodium	1.8	g.
Chloride (as Cl)	3.4	g.
Potassium	5	g.
Iron	36	mg.
Vitamin A	5,000	units
Vitamin B_1	5.3	mg.
Riboflavine	5	mg.
Nicotinic Acid	35	mg.
Pantothenic Acid	13.5	mg.
Choline	334	mg.
Pyridoxine (B_6)	1.9	mg.
Vitamin B_{12}	10	micrograms
Vitamin C	45	mg.
Vitamin D	1,000	units
Vitamin E (acetate)	24	mg.
Vitamin K	5	mg.

Plus trace requirements.

Available in 1 lb. (450 g.) tins.

Further Particulars from the Manufacturers: Glaxo Laboratories (S.A.) (Pty.) Limited, P.O. Box 21, Wadeville, Transvaal.

THE THERM-O-RITE HYPO-HYPER-THERMIA UNIT

Westdene Products (Pty.) Ltd. provide the following information:

The *Therm-O-Rite Hypo-Hyper-Thermia* Unit was designed for the purpose of replacing ice bags, or ice baths and hot water bottles when applying *cold* or *heat* to patients who required prolonged and/or extensive applications of either; and as important, also to provide a scientific method of applying *exact temperatures*.

While the emphasis is usually placed upon the *use of cold in medicine and surgery*, attention is called to the fact that the *Therm-O-Rite Hypo-Hyper-Thermia* Unit and Applicators provide a convenient and effective method for applying *High, intermediate or low temperatures*.

The Applicators are made in various sizes and shapes for efficiency and convenience in applying a *desired* temperature to the whole body or to any external part. They are flexible, and can be adjusted to patients of quite dissimilar size—making for economy in the number and variety required for a complete hospital service. The Blanket Type Applicators are used for generalized refrigeration, i.e. for thoracic, cardiac, cardiovascular and neuro-surgery. They may also be used for the reduction of many types of hyperpyrexia and in the treatment of shock by the reduction of the body temperature of 2°–4°.

Applicators providing for localized refrigeration are also available.

Localized radical refrigeration has the unique power to *control* simultaneously *pain, shock, exudation, infection and tissue devitalization*.

Some of the accepted uses for localized refrigeration are:

Anaesthesia for amputations; preservation of limbs for long or short periods; crush injuries, thrombosis and embolism; burns and frost bite; treatment of peripheral vascular diseases; orthopaedic operations; relief of pain, sciatic or neuritic.

PREPARATE EN TOESTELLE

DIAGNEX BLUE VIR BUISLOSE MAAGONTLEDING

SQUIBB SE ASUUR A-KARBAKRIELHARS DIAGNOSETOETS

Diagnex Blue maak dit moontlik om maagsurigheid op 'n eenvoudige kwalitatiewe wyse vas te stel sonder die noodsaaklikheid van intubasie.

Al die benodigdhede word verskaf in die *Diagnex Blue-pakkie*, en die metode bestaan uit 'n eenvoudige verandering van die asuur A-verfstof van die indikatorhars vir die waterstof-ione van vrye soutsuur in die maag. Die vrygestelde verfstof word in die bloedstroom opgeneem en saam met die urine afgeskei. Die verfstofinhoud (wat met die maagsuur ooreenstem) kan vasgestel word deur 'n blote-oogvergelyking met kleurstandaarde.

Breë Nuttigheidsbestek: Die gebruik van *Diagnex Blue* in die spreekkamer, kliniek of hospitaal is besonder voordelig vir die besige geneesheer, want dit bespaar nie alleen veel tyd nie maar verlos die pasiënt ook van al die ongerief van maagintubasie. Daarbenewens het 'n onlangse inleidingsartikel in die J.A.M.A. ook daarop gewys dat die eenvoud en besuiniging van die *Diagnex Blue*-toets dit 'n waardevolle hulpmiddel maak vir die massa ondersoek van 'n groot aantal mense vir opname-doeleindes.

Beskikbaarstelling: Die individuele *Diagnex Blue*-eenheid bestaan uit 'n pakkie met 2 gram verfstofhars wat ongeveer 100 mg. asuur A-verfstof bevat. In 'n afsonderlike omhulsel is daar twee tablette bevattende 250 mg. kaffeïennatriumbensoaat per tablet. Gebruiksaanwysings vir die pasiënt en etikette vir urine-versamelingsbottels word ook verskaf.

Iedere pakkie wat 5 toetse bevat, sluit ook in 'n vergelyker vir die uitvoering van die blote-oog-toets.

Voorrade is verkrygbaar by alle groot- en kleinhandelaars.

Vervaardigers: Squibb Laboratories (Pty.) Limited, Pharmacy-gebou, Jorissenstraat 80, Braamfontein, Johannesburg.

PABRACORT

Die *Pabracort* (hidrokortisoonasetaat)-inblasingstoestel word aangedui vir die behandeling van hooikoors (seisoensrhinitis), allergiese rhinitis en ongekompliseerde allergiese asma. 'n Onlangse verslag in die *Lancet*, gedagteken 25 Januarie 1958, bl. 187–188, toon aan dat 70% van 'n groep kroniese asmalyers met welslae behandel is.

Werkingsmetode. Hidrokortisoon onderdruk die sel- en vog-elemente van die ontstekingsreaksie, en is veral doeltreffend as die ontsteking aan allergiese faktore alleen te wyte is. Absorpsie uit die neusslymvlies in gevalle van allergiese rhinitis is voldoende om die gelyktydige oogbindvliesontsteking te laat bedaar, en om die meegaande allergiese asma te verlig. Maksimum-konsentrasie word bewerkstellig by die plek van die letsel, en skadelike newereaksies soos spysverteringskwale, word vermy deur die plaaslike gebruik van klein dosisse.

Kontra-Indikasies: In die aanwesigheid van openlike infeksie behoort hidrokortisoon nie gebruik te word sonder geskikte antibiotiese of chemoterapie nie.

Toediening: Aangesien hooikoors 'n betreklik gelokaliseerde openbaring van allergie is, is plaaslike aanwending deur middel van inblasing ideaal. Om welslae te verseker, is dit nodig dat 'n baie fyn verdeelde poeier (gemiddelde grootte van die deeltjies: 5 mikron) gebruik moet word sodat egalige verspreiding en die allernouste kontak tussen hidrokortisoon en die ontsteekte slymvlies met minimum-prikkeling bewerkstellig kan word.

Aanbieding: Soos afgebeeld.

Pabracort-hervulkapsules is ook verkrygbaar in bottels van 10.

Pabracort word beskikbaar gestel soos hierbo, maar kan ook gebruik word as 'n *inaseming* vir die behandeling van chroniese asma.

Vervaardig deur Paines & Byrne Ltd., Greenford, Engeland, en Bemark deur die Alleenverspreiders vir Suid-Afrika: Petersen Beperk, Posbus 38, Kaapstad, en Posbus 5785, Johannesburg, by wie nadere besonderhede verkrygbaar is.

COMPLAN

'N NUWE DIEETKUNDIGE HULPMIDDEL VIR HUIS- EN HOSPITAALGEBRUIK

Complan bied u 'n eenvoudige oplossing van die probleem van doeltreffende voeding wanneer 'n normale dieet nie geneem kan word nie. Een pond (450 g.) *Complan* verskaf 2,000 kalorieë, ewewigtige hoeveelhede proteïene, koolhidrate en vetsoorte, en al die vitamiene, minerale en spoorvereistes. Dus, as hoegenaamd geen gewone voedsel geëet kan word nie, kan een pond (450 g.) *Complan* per dag, toegedien deur 'n buis of met 'n kannetjie, die pasiënt 'n onbepaalde tyd lank aan die lewe hou. As die normale opneming van voedsel beperk word, is kleiner hoeveelhede *Complan* 'n waardevolle dieetkundige toevoegsel.

Complan word maklik toegedien. Meng dit eenvoudig met water, en dit is gereed om aan die pasiënt gegee te word. *Complan* het 'n aangename smaak wat dit besonder aanneemlik maak as dit met 'n kannetjie toegedien word, en, aangesien dit 'n lae vetinhoud het en vry van stysel en koringgluten is, word dit merkwaardig goed verdra selfs deur pasiënte wie se spysverteringstelsel verswak is.

Complan in die Hospitaal: Dit is veel makliker om 'n volledige, vryvloeiende buisvoeding of 'n nieprikkelende vloeibare dieet met *Complan* voor te berei as met die normale metodes, en dit neem minder

tyd in beslag. Ander spesiale diëte kan makliker voorberei word met *Complan* omdat die hoeveelheid van iedere voedselbestanddeel wat daarin voorkom, haarfyn bekend is.

Complan los ook die probleem op van 'n geskikte dieet vir invalides, herstellendes en andere wat nie in staat is om normale maaltye te geniet nie en by die huis verpleeg word.

Geen ander voedselsoort bied so 'n volledige antwoord op so baie voedingsprobleme nie.

Complan kan toegedien word:

(*a*) *As 'n buisvoeding;* (*b*) *As 'n ononderbroke indrupping in die maag;* (*c*) *As 'n drankie wat met 'n kannetjie toegedien word;* (*d*) *Saam met ander voedsel.*

Indikasies: (*a*) *As Enigste Dieet*: Bewustelose pasiënte, bv. na 'n aanval van beroerte, 'n kopbesering of neurochirurgie; pasiënte wat nie in staat of bereid is om te sluk nie, bv. in gevalle van bulbêre verlamming wat deur poliomielitis veroorsaak is, en tydens geesteskrankheid; na operasies, veral operasies aan die spysverteringskanaal; na plastiese of kaak- en gesigschirurgie of brandwonde; gastrostomie-gevalle; pasiënte wat aan swere ly, bv. as 'n alternatief vir melk vir ononderbroke indrupping in die maag, en as 'n nie-prikkelende vloeibare dieet.

(*b*) *As 'n Aanvullende Dieet*: Vir invalides, herstellendes en bejaardes wanneer die opneming van voedsel beperk is; verwagtende en sogende moeders, groeiende kinders, babetjies wat voor die tyd gebore word, en wanneer ekstra voedingstowwe benodig word; spesiale diëte wat 'n hoë proteïen-vitamien-mineraal-opneming vereis.

Die Complan-Formule (per Pond):

Proteïen	140	g.
Vet	74	g.
Koolhidraat	200	g.
Kalsium	3.8	g.
Fosfor	3.6	g.
Natrium	1.8	g.
Chloried (as Cl)	3.4	g.
Kalium	5	g.
Yster	36	mg.
Vitamien A	5,000	eenhede
Vitamien B_1	5.3	mg.
Riboflavien	5	mg.
Nikotiensuur	35	mg.
Pantoteensuur	13.5	mg.
Cholien	334	mg.
Piridoksien (B_6)	1.9	mg.
Vitamien B_{12}	10	mikrogram
Vitamien C	45	mg.
Vitamien D	1,000	eenhede
Vitamien E (asetaat)	24	mg.
Vitamien K	5	mg.

Plus spoorbehoeftes.

Verkrygbaar in blikke van 1 pond (450 g.)

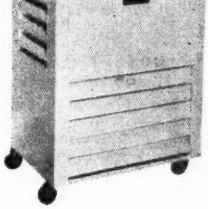
Nadere Besonderhede is Verkrygbaar van die Fabrikante: Glaxo Laboratories (S.A.) (Pty.) Limited, Posbus 21, Wadeville, Transvaal.

DIE THERM-O-RITE HYPO-HYPER-THERMIA-EENHEID

Westdene Products (Pty.) Ltd. verstrek die volgende inligting:

Die *Therm-O-Rite Hypo-Hyper-Thermia*-eenheid is ontwerp om yssakke of ysbaddens en warmwatersakke te vervang in die geval van pasiënte wat met *koue* of *hitte* behandel moet word, en waar die langdurige en/of uitgebreide aanwending van een of die twee noodsaaklik is. Van ewe groot belang is die feit dat die eenheid die geneesheer 'n wetenskaplike metode bied om die pasiënt teen *presies die regte temperatuur* te behandel.

Terwyl die klem tydens geneeskundige en chirurgiese prosedures gewoonlik op die gebruik van koue val, word die aandag gevestig op die feit dat die *Therm-O-Rite Hypo-Hyper-Thermia*-eenheid en -applikators die geneesheer 'n gerieflike en doeltreffende metode vir die aanwending van hoë, middelmatige en lae temperature bied.



Die applikators word in verskillende groottes en fatsoene gemaak vir die doeltreffende en gerieflike aanwending van enige *verlangde* temperatuur op die liggaam as 'n geheel, of op enige uitwendige deel daarvan. Hulle is buigbaar, en kan by pasiënte van verskillende liggaamsgroottes aangepas word. Gevolglik word besuiniging in die hand gewerk wat betref die aantal en die verskeidenheid wat vir 'n volledige hospitaaldiens nodig is. Die Applikators van die Komberstipe word gebruik vir algemene verkoeling, d.w.s. vir borskas-, hart-, kardiovaskulêre en neurochirurgie. Hulle kan ook gebruik word vir die vermindering van verskillende soorte hiperpireksie en by die behandeling van skok, want hulle is in staat om die liggaamstemperatuur met 2°–4° te verminder.

Applikators vir gelokaliseerde verkoeling is ook verkrygbaar. Gelokaliseerde radikale verkoeling besit die unieke vermoë om pyn, skok, uitsweetvog, infeksie en weefselverswakking tegelykertyd te kontroleer.

Hier volg 'n paar van die aanvaarde gebruike vir gelokaliseerde verkoeling:

Anestesie vir amputasies; die behoud van ledemate vir lang of kort tydperke; verbryselingsbeserings, trombose en embolisme; brandwonde en bevriesing; behandeling van randstandige vaatkwale; ortopediese operasies; verligting van heupjig en senuweepyn.

CORRESPONDENCE

PLASMA VERSUS DEXTRAN

To the Editor: In your Editorial of 23 November 1957, the statement 'not one of the plasma substitutes so far offered can be regarded as adequate' is misleading to say the least. This Editorial goes on to support the use of plasma on the grounds that, in addition to the plasma proteins, it contains antibodies, enzymes, clotting factors, buffering capacity, etc. The most important indication for plasma or a substitute is acute hypovolaemia. In this condition life can be saved by the rapid infusion of a

plasma expander. Plasma is effective in these circumstances by virtue of the plasma proteins it contains; some of the other factors cited above should be considered as unavoidable and potentially dangerous constituents. There is certainly no evidence that another person's antibodies or enzymes are of any value to a shocked patient. I submit that to condone or recommend plasma on the basis of these additional factors is therapeutically unsound. Dextran has been successfully used in quantities which, by now, must amount to millions of bottles for the treatment of hypovolaemic shock. It has been shown to possess many practical advantages over plasma with few of its disadvantages.

Your Editorial entirely neglects the fact that plasma recovered from time-expired blood often possesses a number of undesirable features, such as a high potassium content and a low content of plasma protein. It is not a natural substance, although it is assumed to be by many authorities, for it is heavily diluted with acid citrate glucose, usually to the extent of 100 c.c. to every 150 c.c. of plasma. For this reason, it is a highly acid solution whose buffering capacity is not all that good.

The haemostatic factors mentioned as being present in plasma are mostly extremely labile substances and are, therefore, often absent or only present in very small amounts in plasma recovered from time-expired blood. The haemostatic quality of such plasma is not, therefore, one of its outstanding or constant features. Moreover, because of the excess of citrate in such plasma, it can and does sometimes exert precisely the reverse effect. If clotting factors are required, surely the policy to-day should be to endeavour to isolate all the numerous factors concerned in the complex mechanism of blood coagulation in a pure form from fresh plasma and issue them, for the treatment of patients, as dried, stable, concentrated and standardized preparations known to have a specific haemostatic defect. Where the specific nature of the defect is unknown, the correct treatment is to transfuse with fresh plasma or fresh blood in which the anti-coagulant employed is neutralized by the body.

The Editorial refers to antibodies in plasma. In most cases, the quality and quantity of these are unknown and, anyhow, it is seldom administered because of these properties. Furthermore, some of the antibodies present in normal plasma such as isoagglutinins, haemolysins and those that can render patients hypersensitive to allergens, are more likely to be harmful than the reverse.

The statement that because plasma has been produced on a unit-for-unit basis, the risk of transmitting homologous serum jaundice has thereby been reduced to that of whole blood, must surely be an error. Allowing nothing for wastage when harvesting, plasma must carry at least double the risk of an equal quantity of blood, volume for volume. Why subject a patient to this danger when a blood substitute such as dextran, which is entirely free from this danger, can be equally well employed?

The production of plasma on a unit-for-unit basis, is not the simple procedure that this Editorial would have us believe. It is not the ideal method of processing plasma, but an expedient that has been forced upon us by the fact that no method of production has yet been discovered that will render plasma non-icterogenic. It is neither practical nor economical to filter plasma produced on a unit-for-unit basis. Complete reliance, therefore, has to be placed on bacteriological tests and cold temperature storage. Furthermore, each unit has to be separately tested which must be very expensive and the tests must be unduly extensive and thorough if no undue risk is to be taken after this material has been dried and issued; nor is it practical to test each unit for pyrogens, total protein and isoagglutinins, as was the practice with filtered pooled plasma. It is also a fact that the isoagglutinin titre of unit-for-unit plasma must be greater than that of pooled plasma, since there is nothing added to such plasma to absorb these antibodies.

The dried plasma material is not entirely stable. It must be kept cool and protected from sunlight and even when stored under these conditions, it will deteriorate slowly. It cannot be completely relied upon in an emergency, since there is no way of telling by inspection whether it is suitable for transfusion until it is reconstituted immediately prior to administration. It must, therefore, be carried in excess quantities and a bottle of reconstituting fluid must be carried with it; this places an extra strain on storage space and transport, both of which may be at a premium in times of emergency. Dextran, however, keeps almost indefinitely under almost any conditions of storage and requires half the space. It can therefore be stockpiled with greater confidence, and it is always readily available. It is cheaper to produce, to store and to transport. It is apyrogenic and free from all danger of transmitting homologous serum jaundice.

It is for these reasons that the Air Ministry have recently issued to the R.A.F. a pamphlet on the treatment of burns in which the use of plasma is decried, and only dextran, supported by blood, is recommended for the treatment of the accompanying shock.

In these troubled times, no country can consider itself as being free from the danger, or outside the range of attack by nuclear or thermonuclear weapons. The first line of defence against such an attack is dispersal of all but key personnel from target areas. This will entail the evacuation of all large towns and cities and the scattering of organized blood donor panels. Even if it is possible for the blood transfusion services to continue to operate under such conditions, blood and blood products will be in short supply just at the time when they may be most required.

The effect of modern weapons, i.e. the atom bomb and the nepalm bomb, is such that the great majority of casualties will be from burns requiring transfusion with plasma volume expanders rather than blood. Of all plasma volume expanders, including dried blood products, dextran is the easiest and most reliable to stockpile against such an emergency. Furthermore, its production and supply can be boosted more quickly than blood or its products.

In conclusion, I would submit to you, Sir, that as dextran will be used on a large scale in times of emergency, it is essential that the medical and nursing professions should be fully conversant with its clinical applications, and be encouraged to remain familiar with its life-saving properties in the emergencies of normal times.

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